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Part I.—Original Articles.

THE TWENTY-SIXTH MAUDSLEY LECTURE:

THE ASSESSMENT OF PERSONALITY.*

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Psychiatry and psychology.—In his preface to *The Pathology of Mind*, Henry Maudsley commented on the peculiarly isolated way in which the study of mental illness had developed during the previous fifty years. "Treatises on mental disorders," he said, "deal with their subject as if it belonged to a science entirely distinct from that which is concerned with the sound mind." This, he continued, is as though a pathologist were to discuss cardiac and respiratory disease, with little or no knowledge of current work on the physiology of the heart or the lungs. And it was one of his chief aims "to put a happy end to the inauspicious divorce between the two sciences."† Partly in the hope of bringing them into closer touch, his discussion of pathological conditions was prefaced by a systematic account of the normal mind: and in the first edition of his work (1867) the two topics were included in a single volume. Nevertheless, in spite of Maudsley's arguments and his excellent example, few writers on mental pathology have, until quite recently, paid much attention to advances in general psychology. When they describe mental processes or characteristics, they constantly fall back on popular concepts or on out-of-date terms which present an incongruous mixture of an obsolete faculty psychology with an antiquated associationism—doctrines that were already under heavy criticism when Maudsley himself was writing.

It might, I think, be reasonably argued that the relation between psychology and psychiatry is similar to that which obtains between psychology and pedagogy. The teacher who has to train the growing mind must know something of the mind's potentialities; and yet, essential as such basic knowledge unquestionably is, the principles of training cannot be merely deduced from those of general psychology, as nineteenth century psychologists so often assumed. The applied science thus forms a semi-independent branch. In the same way the psychiatrist who has to diagnose and treat pathological conditions of the mind must start with a sound scientific conception of mental structure and of mental processes. Yet psychiatry is certainly not, as Stahlbaum once declared, merely a set of corollaries from the general study of mind as such.

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* Delivered before the Royal Medico-psychological Association, November, 1951.

† *Loc. cit.*, p. v; and *The Physiology of the Mind*, 1876 ed., p. vi.

Accordingly, Maudsley's own suggestion—that the pathology of mental disease bears the same relation to psychology as the pathology of physical disease bears to physiology—may, I think, be a little misleading. Somatic medicine, though recognizing the existence of individual idiosyncrasies, is based almost exclusively on the general study of the body and its functions. There is no separate branch of science dealing with individual differences in anatomy and physiology. Although such differences exist, they are assumed to be of small extent and of minor importance. Psychological medicine, however, requires a knowledge, not only of the general structure and working of the mind, but also of the nature and amount of individual variation. Thus, for the psychiatrist an acquaintance with individual psychology is of even greater importance than an acquaintance with general psychology. Nevertheless, it is surprising to note how little attention is devoted in the ordinary psychiatric textbook to what is known of normal individual deviations. How often is unusual behaviour, which the trained psychologist would recognize as the normal reaction of a healthy child to somewhat abnormal situations, interpreted by the psychiatrist as indicative of some pathological disturbance!

Individual psychology and its history.—Current notions about the nature of individual personality, and the most effective methods of investigating it can best be understood if we briefly trace their history. Early efforts at placing the study of individual psychology on a systematic foundation were mainly deductive. The best known and the most influential of such attempts—that originally termed " organology " but later known as " phrenology "—began by formulating six postulates or " laws of cerebral physiology," and from these deduced a plausible scheme of diagnostic symptoms, with little or no systematic attempt at empirical verification. By 1880 experimental work on cerebral localization had entirely discredited the neurological theories elaborated by Gall, Spurzheim, and Combe. Nevertheless, in their descriptions of mental disorders, most medical writers still retained the psychological terminology popularized by phrenological writers, together with a general belief in the doctrine of temperamental types which those writers had adopted and reformulated in physiological terms.

To psychologists with a more philosophical bias, like Sir William Hamilton and his followers, both the faculty school, to which the phrenologists belonged, and the later associationist school which superseded them, appeared to deny or at least to disregard the unified and integrated character of all mental life. Accordingly to avoid the ancient controversies about the unity of the mind and the unity of the self—terms which incidentally had come to imply that every mental process was by its very nature a conscious process—he substituted the term " personality." It is, indeed, to Hamilton that the psychologist is indebted both for the doctrine of unconscious mental activities, and for the far-reaching notion that personality, with its various capacities and tendencies, is essentially an unconscious structure. Meanwhile, the investigation of the simpler mental processes had been rendered more objective and more exact by the experimental and statistical methods introduced into general psychology by Fechner ; and Spencer, Darwin, and Bain were transforming the study of the mind from a branch of philosophy into a branch of biology. Hence, by the time Wundt published the first edition of his famous textbook,* general psychology had been firmly established on an inductive basis.

Personality, normal and abnormal.—The first to apply a similar approach to the investigation of individual differences was Francis Galton, who combined in a unique and original way the standpoint of the biologist, the experimentalist, and the statistician. During the nineteenth century the biological conception of psychology, particularly as developed by Spencer, attracted attention far more rapidly in France than in Great Britain. In that country the ground had already been prepared by Comte's positivist teaching. Maudsley's books were almost immediately translated into French. His insistence on a physiological approach appealed strongly to medical writers, who still adhered to the materialism of La Mettrie, Condillac, and the Encyclopedists ; and Galton's studies of heredity at once aroused widespread interest. Taine's work on intelligence (1870), Charcot's work on nervous diseases (1873), Ribot's work on memory, will, feelings (*les sentiments*) and their various disorders (1881–85), led to the numerous experimental investigations of Binet and his collaborators. Influenced largely by Galton, Binet never tired of insisting that the study of normal deviations must form an essential preliminary to the study of abnormal ; and it was his aim to base the observation of individual characteristics on some well-attested scheme or schedule, and wherever possible to employ Galton's device of mental tests.

Binet's first important contribution was an investigation of the alterations of personality (1891). This was followed by a series of researches on suggestibility, carried out by the aid of ingenious tests, and showing that processes first noted among hysterics were also a common feature of normal mental life. A few years later he commenced his inquiries into the intelligence of normal and defective children. The chief outcome was the celebrated age-scale for measuring general ability among *les normaux* and *les anormaux*. Throughout, his main contention was that "so-called mental defects and diseases are not clinical entities, disorders of this set of organs or of that, as we might suppose from the analogy of bodily disease, but a change in the personality as a whole." That being so, he argued that it is incumbent on the psychiatrist to study human personality as such, including all its physical, intellectual, emotional, and moral manifestations.

With Janet there is a reaction against the exclusively materialistic approach of Charcot and Ribot, and a clear recognition that psychological conditions cannot be adequately described solely in physiological terms. The processes of dissociation and disintegration as contrasted with processes of association and integration, and the study of multiple, split, and alternating personalities, brought the problem of individual organization still more prominently into relief ; but we miss for a while the interest in the dynamics of mental processes which is to be found in Spencer and his followers and becomes still more conspicuous in the speculations of Freud.

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* *Grundzüge der Physiologischen Psychologie*, 1873. It should be noted, however, that, as the very title of Wundt's textbook shows, psychology in Germany was still regarded as a branch of physiology rather than, as in this country, a branch of biology. This standpoint was retained by those psychiatrists who were Wundt's pupils, notably Kraepelin and Bleuler.

Personality and its definition.—During recent years, the term " personality " has come into increasing use among psychiatric writers. Numerous attempts, often somewhat hastily improvised, have been made to describe its essential characteristics and the appropriate methods of assessing it. To suppose (as Dr. Hayford, in common with many writers, apparently does) that personality is " a useful term introduced by psychiatrists to distinguish behavioural characteristics from intellectual " is doubly misleading. In general psychology the word itself has a long and ancient history ; and, as I have briefly indicated, it has been a favourite term with those psychological schools that have recognized the importance of individual psychology as well as general psychology, and have desired to emphasize the distinctive and unique character of each human being. The abstract noun *personalitas* was originally coined by mediaeval Latinists to translate the Greek word ὑπόστασις (*substratum*) when applied to persons rather than things : its technical meaning was " the special or *characteristic* nature " of a person as opposed to his " *generic* nature." The English form seems to have been first used (and used in this way) by Cudworth (e.g., *Intell. System*, 1678, **1**, 597, 750). It becomes almost a key word with Kant and the neo-Kantians ;[*] and, as Allport and others have pointed out, a heightened interest in human personality was especially fostered by the Romantic writers :

> Höchtes Glück der Erdenkinder
> Sei nur die Persönlichkeit.[†]

Later British psychologists, like Ward and McDougall, who opposed the atomistic conceptions of the older associationists and of the physiological writers of their day, made regular use both of the term and of the conception.[‡]

By contemporary writers the word is unfortunately used in several different senses. It may therefore be helpful at the very outset to state, in the shape of a formal definition, what most modern psychologists would understand by it. " Personality " may, I think, be best defined as *the whole system of relatively permanent tendencies which are distinctive of a given individual, and determine that individual's adjustments to the material and social environment.* This definition appears to be in close agreement with literary usage* and with the interpretation given by Warren in his well-known *Dictionary of Psychology* and still more fully discussed by Allport.

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[*] Cf. Kant, I., *Kritik der praktischen Vernunft* (*Ges. Schriften*, V, p. 87) ; Stern, W., *Die menschliche Persönlichkeit*, 1923, p. 20. Since the English word " personality " had acquired so many different meanings, Coleridge tried to substitute the word " personeity " for the traditional philosophical conception.

[†] Goethe, W., *Westöstlicher Divan*, " Suleika " (1814). G. M. Trevelyan especially notes the influence of the romantic novels of Scott : contrasting Gibbon and Macaulay, he observes that, until Scott's historical romances created a popular interest in the psychology of individual character, historians had almost entirely neglected it. Galton, too, observed that he was first attracted to the study of individual personality by Scott's character-studies.

[‡] Cf., for example, Ward, J., *Psychological Principles*, pp. 464 f. For a more detailed history of the term, see G. W. Allport, *Personality : A Psychological Interpretation* (1938, Chap. II).

The definition, as I have phrased it, is intended to embody the following points. First, personality includes not only the individual's mental qualities, but also his physical and physiological characteristics. The notion bequeathed by Cartesian psychologists that a human being may be divided into a body and a mind—as if he were a corpse inhabited by a ghost—leads to an untenable dualism. Physical and mental are two indivisible aspects of one and the same individual organism ; and the word personality conveniently covers both.

Secondly, all forms of mental activity are included, cognitive as well as affective and conative, intellectual as well as emotional and moral. This has always been the customary usage with psychological writers. " Reason," declares Hume in one of his paradoxical moments, " is, and ought to be, the slave of the passions " ; and this celebrated dictum has been quoted by nearly every psychologist since. Yet throughout the nineteenth century British psychiatry showed a preoccupation with intellectual characteristics. Maudsley himself was no exception. Insanity and mental deficiency were regarded primarily as disturbances or defects of reason. Prichard endeavoured to introduce the notion of " moral affective-conative insanity " ; and this in turn led to the conception of " moral imbecility." These conditions were later regarded as disturbances of the " moral sense," the one acquired, the other innate.† It was left to French psychiatrists to investigate and re-emphasize the importance of emotional tendencies, and to include them in their account of *la personnalité*. Partly as a result, both British and American psychiatrists during the present century have swung over to the opposite direction, and have come to use the word " personality " as if it referred to orectic characteristics *as contrasted with* cognitive, not orectic characteristics *as well as* cognitive.‡ I know of no leading psychologist who has acquiesced in such a view.

Thirdly, the relatively permanent " tendencies " which make up an individual personality—the man's "psychophysiological dispositions" as some writers rather cumbrously designate them—are things that we infer, not things that we directly observe. This may seem contrary to behaviouristic principles. Yet in psychology, as in other sciences, we are compelled to make use of inferential concepts in order to organize our observational data. We must, however, beware of slipping into the mistake of the faculty psychologists, and attributing to such concepts a solid reality which they cannot justly claim. Those who like to talk of "dynamic psychology" prefer to describe such hypothetical qualities as mental "forces" rather than as mental "tendencies," though modern science usually avoids the word "force" as carrying with it popular associations that are likely to be misunderstood.

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* The *Oxford English Dictionary* tells us that a " person " is " an individual human being," and that a man's " personality " denotes his " distinctive personal or individual character "—" that quality or assemblage of qualities which makes a person what he is, as distinct from other persons."

† This definition will be found even in so recent a textbook as Tredgold's *Mental Deficiency* (2nd ed., 1914, p. 314). It may be noted that, when it was first published, Maudsley's own work was criticized by several psychological reviewers for " the way the psychology of the emotions is almost wholly ignored." Curiously enough, Maudsley quotes with approval the first part of Bain's textbook—*The Senses and the Intellect*, yet makes no reference at all to the second part, on *The Emotions and the Will* (1859).

‡ As Roback has pointed out, this altered use—which is tantamount to treating " personality " as a synonym for " character "—is prevalent not only among psychiatrists but also among younger psychologists who have been specially influenced by psychiatric writers (*The Psychology of Character*, 1931, p. 530). C. J. C. Earl (" Methods of Assessing Temperament and Personality," ap. Bartlett, F. C., *et al.*, *The Study of Society*), R. B. Cattell (*The Description and Measurement ofPersonality*), and H. J. Eysenck (*The Dimensions of Personality* and *The Scientific Study of Personality*), all accept at the outset of their account what Roback calls " the omnibus definition of personality " ; yet their subsequent discussions are concerned almost wholly with the " orectic aspects." Earl overcomes the apparent inconsistency by saying that the " other fields of personality " are " not so relevant." Indeed, the psychiatric pendulum has swung so far in the new direction that, in many child guidance clinics, the psychologist is supposed to be competent to assess cognitive characteristics only (intelligence and educational attainments), while the psychiatrist alone (we are told) can deal with " personality, that is, with the influence of emotional or dynamic forces on behaviour as a whole."

Fourthly, in describing such tendencies as forming a system, and that system as constituting a whole, I am endeavouring to preserve what might be called the Gestalt view of personality—the view which makes the total personality an integrated unity, something very much more than the sum of separate responses to separate stimuli. Thus, the phrase carries with it an implicit rejection of the atomistic interpretations adopted by the associationist school and their modern descendants, the physiological behaviourists.

Finally, psychology, as a branch of biology, is forced to view the individual, not as a creature existing in isolation, but as an organism interacting with its environment, which, for human beings, is primarily a psychological or social environment. With Spencer, Bain, Sully, and other members of the evolutionary school, "adjustment" became the key word. Apart from the results of gross organic defect, mental abnormality was held to be essentially a manifestation of "maladjustment"—a disturbance in the relations between the individual and his environment, rather than a disturbance residing wholly within the individual himself. Hence the majority of mental "diseases" were regarded, not as clinical entities analogous to physical diseases, but as more or less distinguishable ways in which a particular type of mind would react to a particular type of environmental situation.* The difference is most obvious in dealing with children. The psychiatrist, even to-day, still tends to adopt a purely clinical approach—'clinical' in the literal sense: he thinks of his patient as a personality to be studied in and for himself, as it were from the bedside. The psychologist wants to observe the child's behaviour in his natural environment, at home, in the classroom, or at play. Hence, in assessing the child's personality, his report will include, not only a description of his abilities, emotional tendencies, moral habits, and the like, but also of his material and social environment.†

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* See, for example, Sully, J., *The Human Mind: A Textbook of Psychology*, 1892, I, p. 203, II, pp. 311, 320 f. Sully, who was appointed Professor of Mind and Logic at University College in 1892, established the first psychological laboratory in the country; and McDougall, appointed Director of the Laboratory in 1902, became an active adherent of the biological school. Most of the early British workers in the field of individual psychology were trained under one or other of these teachers.

† This insistence on the importance of social factors was readily taken up by the later French schools of psychology and psychiatry, who had adopted Comte's positivistic and sociological doctrines into which Spencer's evolutionary theories fitted quite well. It does not appear in German and Swiss-German psychology and psychiatry until much later. In German psychology it emerges most distinctly in Lewin's "field theory"; in German psychiatry it appears first in the "psychobiological" conceptions of Adolf Meyer, who in turn had a profound influence on American psychiatry throughout the twentieth century.

The scientific study of individual differences.—As we have seen, the whole idea that an individual personality can and should be studied by psychological methods is comparatively new. The traditional approach of the physician, which goes back to the days of Galen and his forerunners,* assumed that mental peculiarities could best be inferred from physical appearances. The details were restated in current physiological language and systematized in the theory of " diagnostic signs " developed by Gall and the school of " organology." Owing largely to the influence of Combe and Walker, much of it still formed part of the teaching of the medical school at Edinburgh, even during the latter half of the nineteenth century.† The work of Macauliffe in France, of Giovanni and Lombroso in Italy, and of Bauer and Kretschmer in Germany shows how popular the same type of approach has been among certain continental writers.

During the same period, however, there was an increasing number of writers, both medical and philosophical, who maintained that assessment of personality is a task in which scientific methods are out of place. Judgments of individual character could be reached only by intuitive and sympathetic insight, the result partly of an unanalysable talent or gift, and partly of prolonged experience and practice.‡ Even academic psychologists§ were for long inclined to take a similar view. It was the work of Galton and his followers—Sully, McDougall, and their younger pupils—that first successfully demonstrated both the need and the possibility of applying rigorous scientific procedures to the study of individual personality.

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* The doctrine of the four temperaments, resulting from the mingling of four " humours " with antagonistic " powers," is almost universally ascribed in psychiatric textbooks to Hippocrates : but its metaphysical basis is far too speculative to be consistent with the empirical and anti-metaphysical tone of the few genuine Hippocratic tracts ; and the psychological implications are first clearly formulated by Galen. *Physiognomica*, which is traditionally ascribed to Aristotle, appears also to belong to a much later period. Both traditions, together with the later doctrine of " stigma," formed an essential part of the general " doctrine of signatures," which constituted a basic principle in mediaeval medicine.

† Maudsley explicitly accepts the underlying principle : cf. *Pathology of the Mind*, pp. 178, 322, and index s.v., " stigmata." The surveys of school children carried out by Warner (Hunterian Professor in the Royal College of Surgeons) were based almost exclusively on the inspection of diagnostic signs and stigmata, including size and shape of skull, " facial expression," body-build, and various physical " nerve signs " : (cf. *Mental Faculty*, 1890, ch. IV, VIII). As late as the first decade of the present century many teachers and school medical officers still accepted the diagnostic methods outlined in such books as *Scientific Phrenology* (1902) by Bernard Hollander, M.D.

‡ Jevons' condemnation was continually quoted. " A friend may identify a face. But faces are unique, and who shall classify them ? In spite of all the boasted powers of science, we cannot truly apply scientific methods to our own minds or characters, even though they are more important to us than the nebulae and stars " (*Principles of Science*, 1873, p. 734). A similar view is still urged by many well-known psychiatrists at the present day. Dr. Maberly, formerly Medical Director of the Child Guidance Council, perhaps expresses this view most clearly. Protesting against the notion that (as he puts it) " the entire personality must, and can be, studied by scientific methods," he maintains that " personality can *only* be judged subjectively ; neither scientific method or psychological analysis is an appropriate instrument " (" The Personality of the Problem Child," *Brit. J. Educ. Psychol.*, **16**, 1946, pp. 5 f.).

§ Of these perhaps the last and most eminent was James Ward. To him we owe one of the most suggestive discussions of personality and its development. Yet it is clear that he remained extremely sceptical of " methods experimental and statistical which essay to graduate and even to correlate," and " of an ideal that is idiographic, not nomothetic." Stern's celebrated volume on *Individuelle Psychology* he describes as a " reductio ad absurdum " of " psychography " : cf. more particularly his posthumous volume, *Psychological Principles*, 1918 (an exposition of the famous article in the *Encyclopaedia Britannica* of 1855), p. 433.

Galton's two main contributions consisted in the introduction of (i) the experimental method of mental tests (which included character tests as well as cognitive tests—the best known being the method of free association) and (ii) various statistical devices such as grading impressionistic judgments on a normal scale and above all the measurement of concomitant variation by a coefficient of correlation. The results obtained by these methods quickly showed that mental characteristics could best be inferred from mental symptoms, not from physical, that for cognitive characteristics quantitative standardized tests were far more trustworthy than impressionistic judgments, and finally that, where trustworthy tests were not available, impressionistic judgments could still be greatly improved by means of statistical devices and their value objectively ascertained. The ideal procedure should consist in "*analysis* followed by *synthesis*—a double procedure whereby the observer first analyses the individual's distinctive characteristics in terms of variations in common and fundamental elements, with their dynamic interactions, and then seeks to reconstruct a concrete picture or portrait of each unique personality."*

The psychographic scheme.—In investigating a given personality, it is essential to have a systematic plan of work. The principles on which such a scheme should be based were outlined nearly fifty years ago by one of my predecessors at University College, James Sully. His interest lay primarily in the psychology of the individual child, partly because the investigation of the developing personality is at once easier and more important during the earliest stages of life. It is to him more than to anyone else that we owe what he called, in a somewhat specialized sense, "child study" and "child guidance." Criticizing Maudsley's Comtian leanings, he observes that, "while the psychologist is compelled to refer to the bodily organism if he would give a complete account, he cannot make such a reference a *substitute* for psychological explanation." Accordingly, he prefers to follow Galton, who has already "made a step towards framing a scheme of psychical measurement." At the same time he reminds us that, in the mental field, measurement appears possible only "in certain directions and up to a certain point": it aids us chiefly in the preliminary stage of "analysis," particularly in what he calls the "cross section" (the assessment of the personality as it appears at the present moment). But this must be supplemented by a "longitudinal section," i.e., a full case history to reveal not only apparent causes, reaching back into the past, but also apparent trends, likely to affect the individual's future. Then, having analysed his mind into its constituent characteristics, and having assessed their strength and influence, we have to fit together and re-synthesize these tendencies into an intelligible whole. That means that we must consider how the various factors or components interact—how well they are mutually adjusted, to what extent they conflict, how far the conflicts have been solved or left unsolved, what is repressed, what is sublimated, and so forth.†

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* Cf. Bain, A., *On the Study of Character*, 1862; Galton, F., *Inquiries into Human Faculty*, 1883; Sully, J., *The Human Mind*, 1892, **2**, pp. 302 f.

† Cf. *The Human Mind: A Textbook of Psychology* (1892), vol. **1**, pp. 24–33, and vol. **2**, chap. XIX. The inspiration for Sully's Child Study Association (1895), as well as for Witmer's Psychological Clinic (1896), came ultimately from Galton. The phrase "child guidance" was introduced as a literal translation of the Greek word "paed-agogy" ("the scientific guidance of the individual child"). See Keir, G., "A History of Child Guidance," *Brit. J. Psychol.*, **22**, 1952, pp. 5–29.

In order to know what are the main determining characteristics that we are called upon to estimate, we must possess some acquaintance with the general structure of the mind—what Maudsley himself called "the plan of the mind's development."* Too often the descriptive psychologist (and the psychiatrist when he is attempting psychological descriptions) is disposed to seize on the few outstanding points in each particular case, trusting mainly to experienced insight and following some roughly improvised scheme, or perhaps no scheme at all; and he commonly sets down his observations partly in terms of a semi-popular vocabulary derived from older psychological doctrines that are hopelessly crude and out of date, and partly in terms of a pseudo-Greek jargon that imparts a scientific glamour to unscientific ideas.

Classification as a factorial problem.—The first requirement for a clear and scientific account of any given personality is a rational procedure which enables us both (*a*) to classify the various qualities to be assessed and (*b*) to classify the various persons on the basis of such assessments. For this purpose students of normal psychology have developed an invaluable instrument of research, namely, the statistical technique generally known as "factor analysis."† Very much the same twofold problem confronts the psychiatrist; and perhaps the most helpful thing I can attempt in an introductory survey such as this is to show how the same procedure may be used with advantage in dealing with the psychology of the abnormal individual.

In mental pathology "the most difficult problem," says Maudsley, "is the initial problem, that of classification."‡ In other branches of science the most satisfactory modes of classification are those based on causation. In theory no doubt, that also holds good of mental pathology. Whenever we can show that a certain fairly constant syndrome (e.g., mental deficiency associated with epiloia or with phenylketonuria, or psychotic changes followed by mental deterioration and paralysis) can be accounted for as the effect of a single gene or of a specific micro-organism, then the conditions so produced can be assigned forthwith to an appropriate etiological group. But with the majority of mental disorders the causation is highly complex and to a large extent unknown. The traditional lists of causal categories sketched out by Morel, Meynert, and their later followers were in the main deduced from physiological or pathological hypotheses resting more on plausible conjecture than on empirical research. Thus what Maudsley wrote eighty years ago still remains broadly true: every classification that has hitherto been put forward is little more than "a convenient scheme for grouping together, in some sort of order, phenomena which resemble one another."*

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* *Physiology of Mind*, pp. xii, 121.

† Factor analysis is essentially a statistical device for securing the best available scheme of classification. Its invention is due, not to Spearman (as is so widely supposed), but to the earlier work of Karl Pearson. Pearson's method was first put forward in connection with Galton's problem of classifying and identifying criminals from the records of their physical characteristics. The Bertillon system had proved unsatisfactory; and Galton originally invented his coefficient of correlation (a fractional index for measuring the frequency or extent of concomitant variations) as a means of dealing with this practical task. To deal with a multiplicity of correlated variables, Pearson elaborated what is sometimes known as the "method of principal components," from which, directly or indirectly, all later factorial procedures have since been derived (see Pearson, K., *Phil. Mag.*, **2**, 1901, pp. 559–572, and Macdonell, W. R., "Criminal Anthropometry and the Identification of Criminals," *Biometrika*, **1**, 1902, pp. 177–207), with Pearson's note.

‡ Its difficulty is most strikingly shown by a recent analysis of reports on the pychiatric examinations carried out among recruits for the services during the recent war: e.g., in a study of 100,000 men examined at all U.S. Army induction stations in August, 1945, the number rejected on psychiatric grounds varied at different stations from under 1 per cent. to over 50 per cent.; and of those rejected the numbers classified as psychoneurotic varied from 3 per cent. to 90 per cent. and as psychopathic from 0 per cent. to 81 per cent. (Stouffer, S. A., *et al.*, *Measurement and Prediction*, 1950, ch. XII–XIV, esp. p. 475).

Of these "phenomena" the most readily observable are the more conspicuous signs and symptoms—the *diagnostic* characteristics. But from a practical standpoint it is important to include those that are indicative of the subsequent development of the case—the *prognostic* characteristics. The clinician, confronted with a new patient, usually proceeds, as Kraepelin remarks, somewhat like a botanist confronted with a strange plant. By a method of "progressive delimitation," he determines first its "order," then its "family," then its "genus"—so far no very difficult task. To decide the "species" he has then to consider the "differentiae"; and, in psychiatry as in botany, this differential diagnosis constitutes the hardest step. But the whole procedure suggests the need for what the logician would call a "hierarchical" classification—broad groups, subclassified into narrower groups, each of these again being subdivided into still narrower subgroups.

Classification is essentially a problem for scientific research. But the success of such research will depend on the use of an appropriate scientific method. For investigations into mental conditions the methods so successfully adopted in dealing with bodily disease will no longer serve, largely because the distinctions are by no means so clear-cut. Hence some form of statistical analysis is essential. In dealing with mental subnormality in the cognitive sphere, the classification of general and special disabilities has been greatly assisted by factorial techniques; and in an early paper I ventured to suggest that the same type of procedure might help to overcome the difficulties of classifying psychoneurotic and psychotic disorders.†

So far as I am aware, the first to apply these new statistical methods to observations on adult patients in mental hospitals was Dr. Bernard Hart. Even before the last war, my assistant, Dr. Stephenson, carried out a number of suggestive studies of this kind at the Maudsley Hospital and elsewhere. And more recently the work on "dimensions of personality," undertaken there by several of my former students—Dr. Eysenck, Dr. Lubin, Dr. Clarke, and others—technical as it must appear to the non-mathematician, has aroused considerable interest and not a little controversy.

There is, however, an obvious difficulty to be considered first of all. Factor analysis was devised to deal with quantitative variables, like height, weight, intelligence, and the results of graded tests; and, as ordinarily used, it is applied to tables of correlations obtained from such variables taken two at a time. But in medical practice the observations generally made relate chiefly to the presence or absence of certain symptoms or conditions, and graded measurements are exceptional. The data are qualitative not quantitative, and express differences in kind, not differences in degree, hence, we are told, they are quite unsuited to correlational techniques. Medical writers are particularly apt to raise this objection.* Nevertheless, it seems devoid of any real foundation. It is always possible to calculate the frequency with which the relevant symptoms, taken in pairs, are observed ; and there is no reason whatever why precisely the same factorial procedure should not be applied to frequencies just as well as to coefficients of correlation.

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* *Pathology of the Mind*, p. 296; cf. p. 329.

† *Brit. J. Med. Psychol.*, **17**, 1938, pp. 158 f.

However, this mode of factorization has seldom been used for psychiatric data, and still seems unfamiliar even to many psychological factorists.† Accordingly, by way of demonstrating both the possibility and the value of such methods in psychiatric research, may I give a simplified illustration?

An illustrative instance.—Among children referred at an early age to the psychologist for examination and advice, a large number usually exhibit a mixture of emotional disturbances with behaviour disorders. Of these an appreciable proportion, if their condition is neglected, tend to develop either definite psychoneuroses or serious habits of delinquency. In the course of my work for the L.C.C., it became desirable at an early stage to determine, on the basis of objective evidence, whether such incidental observations could be taken as demonstrating the existence of two genuinely distinguishable types of case, and, if so, how these types could be recognized.

To answer such questions it was quickly found that information relating solely to the child himself—measurements of ability, assessments of temperamental characteristics, and so forth—was insufficient. The ideal procedure would be to secure graded assessments for every relevant condition—family history, home circumstances, as well as for the distinctive characteristics, physical, intellectual, emotional, and moral, of the child. That, however, would entail extensive, prolonged, and repeated inquiries ; and the busy psychologist is disinclined to embark on elaborate investigations of this sort except for the older and more serious cases—cases, that is to say, in which the signs of maladjustment have already become unmistakable, and habitual types of reaction already been formed and fixed. For more general purposes what is needed is some practical means of deriving a rough prognostic assessment from the restricted data available at the first interview. Now, in general, such data—as a glance at the card-indexes will reveal—consist of little more than a statement that such-and-such commonly recurrent conditions are present or absent. The notes of the social worker usually indicate whether certain features were or were not observed in the family history and in the home; and similarly, the school medical officer, the teacher, and the interviewing psychiatrist all usually report their observations on the child himself in simple affirmative or negative terms.

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* Often it seems part of a more general feeling that statistical analysis of any kind is out of place in clinical psychology. For this see Dr. Alan Maberly's criticisms of " statistical psychologists " in the " Symposium on Personality," *Brit. J. Educ. Psychol.*, **16**, 1946, pp. 5–12. A more detailed discussion of the objections will be found in Dr. E. G. Chambers' article, which has so often been quoted (" Statistics in Psychology," *Brit. J. Psychol.*, **23**, 1949, pp. 189 f.) : they are summarized in a non-technical fashion by Dr. B. H. Kirman in his recent book on *This Matter of Mind* (1951, pp. 42 ; Dr. Kirman's account of Karl Pearson's work, however, shows considerable confusion ; in several places he attributes to Pearson the views and methods which Pearson himself most vigorously opposed.) To make a " school " of those psychologists who use statistical methods to check their inferences and dub them " statistical psychologists " is rather like classing all surgeons who publish the results of their operations in numerical tables as " statistical surgeons." As Dr. Bradford Hill observes, statistical analysis is no more than an " aid to clear and logical thinking and the detection of inadequacies in the recorded data." On the general value of statistical procedures in medical research, and for an account of the basic techniques, see his *Principles of Medical Statistics* (1937).

† For example, Dr. Eysenck in a recent publication insists on the need for quantitative data. It is, he asserts, the only type of data lending itself to factorial analysis. Guttman and Lazarsfeld both appear to hold that factorial procedures are not applicable to qualitative material. The few writers who have attempted to factorize qualitative data (by which I mean data allowing two categories only—present or absent, pass or fail, and the like) have tried to express the relations in correlational form by using the tetrachoric coefficient—a process which has been strongly criticized.

In the hope, therefore, of ascertaining whether any provisional classification or forecast could be derived from crude and meagre information of this type, I tabulated the records for a large number of cases, and then carried out a factorial analysis of the frequencies for the conditions most commonly mentioned. To check the validity of the procedure, I selected cases in which each child's subsequent progress had already been followed up, and the precise nature of the disorder had been pretty clearly established.* In one of the earliest investigations, my colleagues and I collected 100 cases in which serious or recurrent delinquency eventually developed, and 200 cases in which a definite psychoneurosis was subsequently diagnosed. Mixed cases, falling into both categories, were, so far as possible, excluded. The problem was to see whether we could determine, from the initial reports and the first brief interview, in which of the two categories the child should be placed. The fact that there was or was not a brief history of occasional theft or wilful disobedience, or that the child had impressed the interviewing psychologist or psychiatrist as an aggressive extravert or an over-anxious introvert, turned out to possess but little predictive value: it was the pattern of data, taken as a whole, that provided the most accurate forecasts.

Here my purpose is not to show the importance of the conclusions actually reached in this particular study, but merely to discuss an issue that is at once simple, definite, and intelligible, and allows of a convincing check. In order to illustrate the nature of the statistical procedure, I shall therefore reduce the inquiry to the simplest terms, and restrict myself to the four indicative clues which, as the fuller analysis showed, had the highest predictive value of those most commonly reported under the four main headings.† They were the following:

A. As regards the material condition of the home: the presence of poverty.

B. As regards the moral condition of the home: unsatisfactory discipline.

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* The figures are taken from an L.C.C. Memorandum on "After Histories of Children referred to Child Guidance Clinics," where the procedure was described in greater detail. The cases discussed consisted of pupils between the ages of 6 and 9 attending the Council's schools and referred to various clinics or centres in London (not only to the Council's own doctors or psychologist). For assistance in collecting and in sorting the data I am much indebted to Mr. R. A. Newcomb and Miss E. M. Hastings. In the record sheets prepared for me, each child was identified by a code number only. Hence I was quite unaware of his later history or appropriate classification until my own assignment was completed.

† There are no doubt other clues that have a still greater prognostic value in themselves. Their absence from the list is chiefly explained by the fact that they are seldom recorded or noted until a later stage.

C. As regards the family history: emotional instability in the relatives.

D. As regards the child himself: a history of disturbed sleep (i.e., frequent nightmares, insomnia, sleep walking, etc.).

TABLE I.—*Frequencies of Orders* 1 *and* 2.

Number of Cases in which the Conditions Specified were Reported (1) Singly (N) and (2) in Combination (Pairs).

Condition.	N.	A.	B.	C.	D.
A. Poverty	132	(58·2)	64	59	65
B. Unsatisfactory discipline	140	64	(82·7)	51	53
C. Unstable relatives	139	59	51	(75·4)	86
D. Disturbances of sleep	151	65	53	86	(99·1)

Table I shows the frequencies with which each of the four conditions was associated with the rest (the frequencies of " Order 2 " in Yule's terminology). It has the form of a correlation table; but the method does not require the frequencies to be actually converted into correlation coefficients.* The *observable* frequencies consist only of what are technically termed " combinations without repetition." For the purposes of factor analysis, however, we also need the " combinations with repetition."† These will be inserted in the main diagonal of the symmetric table; and will thus be analogous to the " communalities " of ordinary factor analysis. Now the present problem seems to be clearly one in which " specific factors " peculiar to each condition have to be assumed. Accordingly, the values inserted in the diagonal must be " reduced values." They can be estimated in the usual way by successive approximation, and are shown in brackets.*

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* Since the use of frequencies rather than correlations has recently been criticized, a further word of explanation is perhaps required. With frequency data, the choice of the best coefficient of correlation or association has always been a point of controversy; and for this reason alone it seems preferable, wherever possible, to work directly with the frequencies observed. Yule's mode of dealing with " manifold classifications " is virtually a method for determining how closely a single factor, calculated by " simple summation," will fit a non-symmetric frequency table, and for testing the significance of the residuals by chi-squared (*Introduction to the Theory of Statistics*, 1910, pp. 61–6, and Tables II and III). Factorial methods were first applied to symmetric frequency tables in order to deal with data obtained for psychological characteristics which merely recorded the observable facts in terms of two mutually exclusive categories—pass or fail, delinquent or non-delinquent, ill or not ill, positive type or negative type, etc. During the war it was suggested that a similar procedure might be used as an aid to the allocation of recruits; and a good deal of instructive discussion arose as a result. In a memorandum on the subject, I distinguished two main methods of treatment: (i) working with standardized frequencies, retaining unity in the leading diagonal, and applying Pearson's method of principal components; (ii) working with unstandardized frequencies, inserting estimated reliabilities in the leading diagonal, and using the higher order frequencies to determine the final classification, either by deducing a rotation matrix or by more direct methods. For purposes of psychiatric classification, the latter mode of approach appears the more suitable. An illustration of a combined use of both alternative principles will be found in a recent paper based on that memorandum (" The Factor Analysis of Qualitative Data," *Brit. J. Psychol. Stat. Sect.*, **3**, 1950: cf. esp. Tables III and IX. For an alternative method of dealing with frequency data, see Slater, P., *J. Roy. Stat. Soc.*, **10**, 1947, 1 and 2 Supp., and Slater, P., and Rao, C. R., " Multivariate Analysis Applied to Differences between Neurotic Groups," *Brit. J. Psychol. Stat. Sect.*, **2**, 1949, pp. 17 f. Mr. Slater would prefer to treat the number of cases as a score, and the differences between normals and different types of neurosis as " differences solely in degree ").

† For the distinction, see any elementary textbook on algebra, e.g., *College Algebra*, p. 403. In a frequency table, as in a correlation table, these estimated values may be regarded as conventional figures expressing the reliability of the assessment so far as it is due to common factors.

TABLE II.—*Factor Saturations.*

Condition.	Unrotated factors.		Rotated factors.		Calculated proportions (per cent.).		Observed proportions (per cent.).	
	I.	II.	I′.	II′.	Delinquent.	Neurotic.	Delinquent.	Neurotic.
A. Poverty	7·47	1·56	4·83	5·93	47·4	42·3	48·0	42·0
B. Unsatisfactory discipline	7·49	4·89	7·99	4·30	78·4	30·8	81·0	29·5
C. Unstable relatives	8·38	−2·28	1·84	8·46	18·1	60·4	21·0	59·0
D. Disturbances of sleep	9·38	−3·33	1·34	9·87	13·1	70·5	15·0	68·0

On factorizing this table by Pearson's "method of principal components," we obtain two significant factors. The saturations found are given in Table II (cols. 1 and 2). There is first a "general" factor: its saturations and factor measurements merely indicate the extent to which the conditions and the individuals are typical of the whole composite group. Secondly, there is a well-marked "bipolar factor," i.e., a factor with both positive and negative saturations. It shows that the entire group of individuals can be divided into two subgroups. The saturations for this bipolar factor can be used as approximate weights for weighting the several conditions. On applying them to the figures in the initial record sheet, we can calculate a factor measurement (weighted sum) for each individual. If the measurement is positive, that will indicate that the child belongs to the first of the two sub-groups; if negative, that he belongs to the other.

To determine the precise nature of the two subgroups, we require an independent or external criterion, i.e., we must fall back on evidence outside that contained in the initial table. In this case the interpretation seems clear. In planning the inquiry, it will be remembered, we selected a sample of children who, as their after-histories had shown, developed either into habitual delinquents or into definite cases of psychoneurosis. Comparing the allocation derived from the factor measurements with that indicated by the subsequent case-histories, there is a remarkably close agreement: 87 per cent. of the prognoses based on the initial data, analysed in this way, would have been justified by the child's later development.

When we deal with a larger number of variables, and perhaps have to work out a classification involving more than two subgroups, a more rigorous procedure is necessary. If possible, it is desirable to convert the "general" and "bipolar factors" into "group factors" with positive saturations only. These saturations should indicate the probabilities (i.e., relative frequency) with which the observed conditions are likely to occur in each subgroup. As in ordinary factor analysis, this can be readily done if we can compute a suitable rotation matrix to effect the requisite transformation. There are three obvious procedures : (i) graphic rotation ; this is the least satisfactory ; (ii) successive approximation ; this in my experience commonly yields far better results ; (iii) factorizing frequencies of a *higher order* ; this is usually the quickest method in those inquiries in which no partial associations are operating ; and it would seem to be the most appropriate here.*

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* With a 4 × 4 table a more direct procedure is available. Since only 2 factors are needed, the completed table will have a rank of 2 only, and therefore all the 3 × 3 determinants will be zero. Moreover, if there is no partial association, the table will have the same rank even when bordered by the observed frequencies of order one. This yields a simple set of determinantal equations for computing the diagonal values.

TABLE III.—*Frequencies of Order* 3.

Number of Cases in which Unsatisfactory Discipline was reported in Combination with Two Conditions.

Condition.	A.	B.	C.	D.
A. Poverty	(39·2)	(29·2)	22·0	22·0
B. Unsatisfactory discipline	(29·2)	(25·6)	(24·9)	(27·1)
C. Unstable relatives	22·0	(24·9)	(30·5)	36·0
D. Disturbances of sleep	22·0	(27·1)	36·0	(42·0)
Total	112·4	106·8	113·4	127·1

With only 4 variables there will be only 4 *observable* frequencies of Order 3. Table III shows the frequencies for those cases in which variable B (Unsatisfactory Discipline) forms one of the three conditions found together. This gives 3 of the 4 observed values. Two such tables would therefore give all.

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* For the benefit of the research student familiar with matrix algebra, the general procedure may be outlined in symbolic form as follows : In accordance with the usual notation, let M stand for the $n \times N$ table of initial observations (1 and 0 being used to denote presence or absence) : then the matrix of product-sums $R_2 = MM'$ will give the "frequencies of Order 2." If we divide throughout by N, the fractions may be regarded as expressing the *relative* frequencies or probabilities : (this reduction is unnecessary for our present problem) : similarly, $R_{3i} = MD_iM'$ will give the frequencies of Order 3, where D_i is a diagonal matrix formed from the ${}_i{}^{\text{th}}$ row of M (the diagonal matrix and the i^{th} row will be identical if we are working with probabilities ; cf. *Brit. J. Psychol. Stat. Sect.*, **3**, p. 182). It should be noted that with qualitative variables these higher order frequencies play a part not unlike that of higher moments in a multivariate analysis of quantitative variables (cf. *Factors of the Mind*, pp. 352 f., 468 and ref.).

Now, still keeping to the notation of ordinary factor analysis, let G denote the factor matrix containing the group factor saturations we desire to obtain. Then $R_2 = GG'$; and (by Yule's formula for cases in which partial association is assumed to be absent or negligible, *loc. cit.*, p. 57, eqn. 9) $\mathrm{R}_{3i} = G\,Y_iG'$, where Y_i is a diagonal matrix yet to be determined. On factorizing R_2 by the method of principal components, we obtain $R_2 = LVL' = FF'$, where, as usual, F denotes the saturations for the general bipolar factors, L the orthogonal matrix of normalized latent vectors, and $V = F'F$ the diagonal matrix of latent roots. We can now deal with the frequencies of a higher order in the same way as we should deal with an application of a given set of tests to a second population or sample differing from the first solely by having different variances for the same factors (cf. *Brit. J. Educ. Psychol.*, **9**, 1939, pp. 45 f. and refs.). To obtain G from F we shall have to postmultiply F by a rotation matrix, H say, so that we write $G = FH$ and $HH' = I$. Still keeping to the usual notation, let P denote the matrix of factor measurements, duly normalized, so that all factor variances are given the same value, and let $W = V^{-1}F'$ denote the weighting matrix for the hypothetical factor measurements (P) obtained from the observed measurement (M). Then the symmetric matrix, S, obtained by pre- and post-multiplying R_{3i} by the weighting matrix, will be

$$S = WR_{3i}W = V^{-1}F'R_{3i}FV^{-1} = V^{-1}F'GY_iG'FV^{-1} = V^{-1}F'FHY_iH'F'FV^{-1} = HY_iH'.$$

Thus H and Y_i will be the latent vectors and roots of S, the weighted matrix of higher order frequencies. The values can again be computed by Pearson's method. Having thus obtained H, we can at once determine G from F by postmultiplication. If we desire to avoid the labour of computing principal components by weighted summation, reasonable approximations can be obtained by using simple summation : this will entail the usual changes in the foregoing formulae.

If there are no appreciable partial correlations, the *hypothetical* values can be filled in by the determinantal procedure referred to above. The value inserted in the i^{th} row of the i^{th} column will be taken from corresponding tables constructed for the i^{th} variable. The figures estimated in this way are shown in brackets. Using the formula given in the preceding footnote, we can now apply the routine procedure for calculating the requisite rotation matrix.* It proves to be

$$\begin{bmatrix} \cdot 463 & \cdot 886 \\ \cdot 886 & -\cdot 463 \end{bmatrix}.$$

This yields the saturations for two group factors shown in Table II (cols. 3 and 4). The figures make it obvious that, although the two categories are clearly distinguishable, there is (at any rate in this short list—and the same is true of all the conditions included in the larger inquiry) no distinctive set of symptoms always present in one group and always absent in the other. The number of individuals in each sub-group can be estimated by taking the numbers reported as exhibiting the four separate conditions (shown by the figures in col. 1 of Table I), and treating this column as an extraneous variable.† Factor saturations for this variable can be calculated by the usual formula ; their sums are then divided by the factor variance ; and the resulting figures transformed like the rest by means of the rotation matrix. The numbers as thus estimated are 104 for the subgroup represented by the first factor and 196 for that represented by the second factor—a discrepancy of four in each subgroup. However, nearly all these eight cases prove on investigation to be children of somewhat mixed and mild characteristics whose allocation might perhaps be regarded as a matter of some doubt.

In order to calculate the frequency with which the several conditions occur in each subgroup the saturations are multiplied by $\sqrt{104}$ and $\sqrt{196}$ respectively. The percentages as thus computed are shown in cols. 5 and 6 of Table II ; the actual proportions are given in the last two columns. Ordinarily, of course, we should have no such check upon our inferences. But this investigation was planned, not to reach new conclusions, but to test the accuracy of the procedure.

From the new factor saturations we can construct weighting coefficients ("regressions") by the usual procedure ; and in this way we can secure personality assessments for each of the individual children indicating to which subgroup he belongs, or rather—to put it more accurately—the extent to which each resembles a typical member of either subgroup. On comparing the results with the after-histories of the children, *the number of discrepancies now amounts to barely 12 per cent.* All are cases in which the children have low factor measurements, which of itself implies that the inferred assignment was somewhat doubtful. Most of the discrepancies are the result of unforeseeable circumstances; others seem due to errors in the classification used as a criterion; the rest result from the narrow range of the information supplied.

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* With a small number of observed variables, it is desirable to avoid as many estimated values as possible ; and, in cases like the present, the rotation matrix can be calculated by using the non-diagonal estimates only. However, particularly when we have to deal with a large number of variables, the inclusion of the estimated values makes the calculations simpler, and enables us to apply the procedure mentioned in the previous footnote. When the number of observed variables is large, the frequencies of higher order can best be dealt with by what I have called the " sum method of factorization " (*Brit. J. Psychol. Stat. Sect.*, **2**, 1949, Appendix). In that case the complete table will have n^2 rows (in the present case 16 rows), i.e., it will include 4 submatrices of which Table III will be the first. What are then factorized are the sums of the columns in the several submatrices (cf. Appendix, *loc. cit.*, Table VI). Thus at every stage (as I have argued in earlier papers) the procedure is virtually the same as that adopted for the factor analysis of quantitative variables.

† See " Factor Analysis by Submatrices," *J. Psychol.*, **6**, 1938, pp. 346 f.

Let me repeat, however, that for illustrative purposes I have taken an example that is almost absurdly simplified. In more systematic studies, where a larger number of conditions have been included, the allocations prove to be far more accurate. But even this simple example will, I think, suffice to show that the methods of factor analysis may be validly and usefully applied even where (as in so much psychiatric work) we have to deal with what are sometimes termed "qualitative" data as distinct from "quantitative." It will be equally clear that such methods may be used with advantage, not only to predict risks in cases like the present where extraneous influences have to be taken into account, but also for the more general problems of classification, particularly where a miscellaneous set of disorders have to be classified on the basis of intrinsic symptoms only, i.e., of conditions observable solely in the patient. I must, however, repeat that factor analysis should not be regarded as a separate and self-contained technique,* in the way that both its supporters and its critics have been prone to do. It is merely a device for confirming or confuting, and sometimes for correcting or supplementing, hypotheses already tentatively reached on other grounds.

The structure of human personality.—Let us now turn to the main results hitherto achieved by the use of such procedures. In its most comprehensive form, the question which factor analysis was designed to investigate† was simply this. Is there any general ground plan common to all human personalities, or is the mind, as the associationists maintained, a mere *tabula rasa* on which the patterns, unique for each individual, are traced or stamped by personal experience? And if there is a common structure, what are its essential outlines?

So far as such investigations take us, it would seem clear that the mind has a structure, and that its structure is essentially *hierarchical.** Here I can do no more than briefly indicate the scheme which has gradually emerged. It distinguishes first between the broader and more comprehensive tendencies; then divides each of these into tendencies more limited and specialized; and these in turn are subclassified into still more specialized components; until at last we appear to approach the most fundamental and most elementary constituents of mental life.

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* This is perhaps due to a misunderstanding of the way so many writers have formulated the purpose of factorial procedures. "The object of factor analysis," says Thurstone, "is to *discover* mental faculties" (*Vectors of Mind*, p. 53, my italics): and so the factorist will often take a set of data already procured with some quite different purpose in view (cf. *ibid.*, p. 108), and uses them to "discover" the factors of the mind. Indeed, many published contributions are occupied mainly with detailed accounts of the arithmetical work; and the "factors" then obtained are given a hasty improvised interpretation by merely considering what the several tests might be supposed to measure. (For criticisms of this procedure, see *Factors of the Mind*, pp. 30 f. In his later writings Thurstone appears to accept the view that a factorial inquiry should be planned from the outset to verify some tentative hypothesis about what factors will be found.)

† See Burt, C., *Brit. J. Psychol.*, **3**, 1909, pp. 94 f.; here the problem was stated for the cognitive aspect of the mind; it was later extended to the emotional or orectic aspects (1915, *loc. cit. inf.*). By 1923 an affirmative answer seemed clearly established (cf. *id.*, "The Mental Differences between Individuals" (Pres. Add., Psychol. Sect.), *Brit. Assoc. Ann. Rep.*, 1923, pp. 215–239). In that paper I suggested substituting the broader phrase "structure of human *personality*" for the narrow term "structure of the *mind*." However, the views there put forward were for long opposed by Spearman and his followers on the ground that they were tantamount to a revival of the "outmoded doctrine of faculties and propensities."

The broadest divisions may at first sight seem too trite and obvious to have called for special research. But the statistical analysis has the advantage, not only of objectively confirming the familiar distinctions, but also of giving them a more precise (and sometimes slightly unexpected) interpretation, while at the same time it reveals the relative importance of the various items grouped together under each heading. The broadest division of all separates what may be called *extra-personal* from *intra-personal* characteristics. Among the former the most important are the characteristics of the immediate social environment.† Among the latter the main distinction is between the *somatic* and the *mental* components respectively. Then, cutting across this vertical distinction (as we may regard it), there is a horizontal distinction between tendencies that appear to be mainly *innate* and those that appear to be mainly *acquired*, that is, between the genetic components and what are presumably effects of environmental influences operating after birth. Such a distinction is extremely difficult to draw in the case of adults; but with children sufficient evidence is often procurable to make at least a plausible estimate—particularly in cases of mental deficiency.

In most of the traditional schemes, *mental* characteristics are usually subdivided into three main groups or tendencies—cognitive, affective, and conative. Factor analysis, however, suggests that the affective and conative are so closely related that they virtually form a single aspect, variously named "orectic" or "appetitive"; and the results imply that the traditional terms require to be reinterpreted. The word "cognitive" must be taken to cover, not only intellectual but also practical abilities (which are in fact guided by cognition);

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* The view that the mind and central nervous system exhibit a "hierarchical" structure is due primarily to evolutionary writers, like Spencer; but it is strongly supported by pathological evidence (due largely to Hughlings Jackson), by neurological evidence (due largely to Sherrington), and by introspective evidence (mainly contributed by Stout and McDougall). Maudsley, taking the notion partly from Spencer, but partly influenced by Comte, was apparently the first to introduce the concept into psychiatry: (*loc. cit.*, chap. II, pp. 109 f.; cf. chap. VIII, on the "orderly subordination of nervous centres"). Alternative views have been advocated by several living writers: e.g., that the mind, unlike the body, is essentially devoid of structure (Thomson) or that it consists of a miscellaneous set of loosely related "unitary traits" or "primary abilities" (Thurstone). But, on the whole, most of these writers seem now to have qualified their earlier criticisms. Vernon, summarizing his factorial results, discovers "a feature which appears highly characteristic of mental structure, namely, hierarchy," and notes that "Cattell also regards the hierarchical picture as superior to the multiple factor" (of Thurstone). Eysenck states that "a hierarchical view of personality structure akin to Burt's conception of factors and McDougall's theory of sentiments, would appear to account for the known facts better than any other." In America, Allport defends "the conception of a hierarchy of levels" which he believes may provide "much help in understanding the development of personality." Piaget, summarizing his work on children, gives much the same description. For a fuller discussion of the history and development of the theory, see E. M. Moursy, *Brit. J. Stat. Psychol.*, **5**, 1952, pp. 151 f.

† On the analysis of environmental characteristics, see Burt, C., "The Assessment of Personality," *Egypt. J. Psychol.*, **2**, 1946, pp. 1–21, esp. Table I, and *Contributions to Social Problems* (Oxford University Press, 1953).

and the words " appetition " or " orexis " must be taken to cover all forms of emotional tendencies, unconscious as well as conscious. A plausible analogy, which should not be pressed too far, is afforded by thinking of the mind as a kind of machine. In dynamics a machine is defined as " an arrangement for directing the application of energy " ; as such it consists of (i) means for accumulating and transmitting energy and (ii) means for regulating and guiding its release so that work is done. The so-called orectic aspect corresponds to the provision of energy ; the so-called cognitive aspect, to the direction of its aim or application.* Thus re-stated, the contrast is similar to that expressed in Maudsley's dictum : " desires furnish the impulses ; the function of the intellect is regulative."†

Cognitive characteristics.—On the cognitive side, factorial methods have revealed a series of factors of increasing specialization. There is first the broadest factor of all—the general cognitive ability commonly named " intelligence." Then, in nearly all researches which are sufficiently comprehensive, two contrasted factors of somewhat smaller range usually appear—namely, what have been called the " practical " and the " intellectual " : here the antithesis is suggestive of that often denoted by terms like " afferent " and " efferent," or " receptive " and " executive." Further factors indicate four main levels—sensory, perceptual, associative, and relational, each with its receptive and executive aspects. There are still narrower factors, some apparently formal factors, others factors of content, many of them reminiscent of the old-fashioned faculties—the verbal, the arithmetical, the spatial factors, the factor for memory, the factor for productive imagination (or " fluency " as it is sometimes called), and so forth. Even these can be further subdivided. The verbal factor, for example, splits up into a small scheme of sub-factors corresponding very closely with the scheme of verbal defects that Head arrived at in his study of aphasia.‡

Affective and conative characteristics.—It is, however, the study of temperamental and emotional traits, and what may be called the " dynamic " aspect of the mind, that is of greatest relevance to the work of the psychiatrist.§

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* In his book on *The Energies of Men*, McDougall calls the latter " the steering process." Woodworth in his *Dynamic Psychology* (1918, p. 36) prefers the words " drive " and " mechanism." More recently Piaget has been independently led by his experimental studies to re-define the traditional terms in much the same way : " every aspect involves an energetic or affective aspect and a structural or cognitive aspect ; emotion attributes a value to certain ends, and thus supplies the energy needed for action : knowledge or intelligence provides the means, and thus impresses a structure on the resulting action " (*The Nature of Intelligence*, 1950, pp. 4–5).

† *Loc. cit.*, p. xvi ; and chap. VI " On the Emotions or Affections of Mind."

‡ For fuller details, see " The Structure of the Mind : A Review of the Results of Factor Analysis," *Brit. J. Educ. Psychol.*, **19**, 1949, pp. 100–11, 176–99.

§ Two of the three best known textbooks on factor analysis seem to have conveyed the notion that the method is restricted primarily to the study of cognitive abilities. Thurstone's *Vectors of Mind* defines factors as " abilities " ; and Thomson's book is entitled *The Factorial Analysis of Human Ability*. In point of fact, one of the earliest factorial inquiries was an analysis of emotional behaviour : (cf. Burt, C., " General and Special Factors underlying the Primary Emotions," *Brit. Assoc. Ann. Rep.*, **85**, 1915, pp. 694 f.). Holzinger and Harman (*Factor Analysis : A Synthesis of Factorial Methods*, 1941) fully recognize that factorial methods can be applied to emotional conditions, and have refactorized my earlier data, offering an interpretation that closely resembles my own (*loc. cit.*, pp. 176 f.). More recently, two of my own former students, Professor R. B. Cattell and Dr. H. J. Eysenck, have carried out numerous inquiries in the orectic field, with abnormal persons as well as with normal.

Most of the investigations, but by no means all, have been carried out with children; but the more important conclusions appear to hold good of both young and old alike.*

(a) *Normal cases.*—With normal persons, whether children or adults, the following factors appear to have been fully established: (1) a general factor of emotionality, accounting for 35 to 45 per cent. of the total variance; (2) a bipolar factor distinguishing sthenic (unrepressed or extraverted) from asthenic (inhibited or introverted) emotions, and usually accounting for about 15 per cent. of the variance; and (3) a further bipolar factor distinguishing euphoric (or pleasurable) from dysphoric (or unpleasurable) emotions, and accounting for 5 to 10 per cent. of the variance. The existence of a general factor on the orectic side, analogous to "general intelligence" on the cognitive side, was established in the earliest investigations, and has since been confirmed by a number of later writers, including Webb, Oates and Cattell. But the factor which has been most frequently verified is the first of the two bipolar factors, though different writers have favoured somewhat different designations.† It is curious that few investigators appear to have hit upon the third factor—that distinguishing the optimist from the pessimist, *l'allegro* from *il penseroso*; yet it is a distinction which the non-psychological observer draws more frequently than any other. All the factors can be subdivided still further; and the more specialized factors appear to correspond roughly, but not precisely, with what McDougall called "instincts" and other writers "natural urges" or "drives."

(b) *Neurotic cases.*—In the investigations on patients suffering from milder mental disorders, the factor patterns found are in the main much the same as those obtained with normal persons. (1) Most investigators have found a general factor; and many have supposed that it might be regarded as a "factor of neuroticism." However, such a phrase would denote a factor found among neurotic cases only or among traits peculiar to neurotics; and, when normal persons are included in the research, there is no doubt that the general factor is the same in both, namely, a factor for emotional instability. (2) The second is also much the same as before, namely, a bipolar factor distinguishing "extraverts " (or " cyclothymes ") from " introverts " (or " schizothymes "). There is, however, a considerable overlap, particularly among younger children where the different types are less clearly demarcated. (3) The third factor is new. It appears to divide the extraverts into (i) those characterized by strong sexual propensities, joyful moods, and a fondness for company, and (ii) those characterized by aggressive, assertive, and inquisitive tendencies.* Those diagnosed as hysterical usually fall into the first subdivision, and the obsessional and compulsive cases into the second. The introverts are similarly divided into (i) those characterized by fear or anxiety, with a marked degree of affection and a proneness to grief, and (ii) those characterized by submissiveness, liability to disgust, and an excessive desire for comfort. Nearly all the cases of anxiety-neuroses fall into the former group, and the majority of the neurasthenic cases into the latter.

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* Cf. "The Analysis of Temperament," *Brit. J. Med. Psych.*, **17**, 1938, pp. 158 f.; "The Factorial Analysis of Emotional Traits," *Character and Personality*, **8**, 1939, pp. 238–54, 285–99; "The Factorial Study of Temperamental Traits," *Brit. J. Psychol., Stat. Sect.*, **1**, pp. 178–203; and Reymert, M. L. (ed.), "Feelings and Emotions," 1950, pp. 531–51, and refs. A detailed survey of the numerous statistical investigations, with 286 references, will be found in R. B. Cattell, *Description and Measurement of Personality* (1946). He endeavours to distinguish factors representing "sources" (e.g., innate tendencies) from those representing "surface characteristics"; I agree with Vernon, however, that for adults such classifications are bound to be somewhat questionable in the present state of knowledge.

† Binet's terms are "objective" and "subjective"; Cattell's "surgent" and "desurgent"; the distinction was verified by factor analysis some time before Jung popularized the terms "extravert" and "introvert." A few investigations have yielded evidence, not wholly conclusive, suggesting (4) a distinction between susceptibility to (*a*) emotional reactions aroused by and directed towards persons in contrast to (*b*) emotional reactions aroused by and directed towards impersonal situations. This "personal factor" may have some affinities with tendencies which Freud terms "sexual," since he expands the word to cover almost every mode of reacting to other human beings. Whereas the three factors mentioned in the text appear to depend largely on genetic constitution, there is little evidence so far available for genetic influences in the case of the last.

Methods of assessment.—The results I have reviewed indicate the kind of psychographic scheme which might be profitably adopted in studying any individual personality. Let us now inquire what procedures are available for assessing such tendencies or " factors," and how much confidence may be placed in each of the common methods.

The special feature of the psychologist's approach consists in his adoption of experimental and statistical techniques. He is not content with mere casual observations as in an ordinary consultant's interview. He endeavours to develop standardized tests to supplement the clinical examination. And, in deriving his assessments, he is led to use, not a single test for each distinguishable trait, but a combination of results obtained from various sources and by various devices.

1. *Tests.*—For cognitive abilities there now exist a number of fairly trustworthy tests, especially for general ability or " intelligence." But training and experience are requisite to know which tests to use for different purposes and for different types of case, and how to interpret the results obtained. Tests for what I have described as the orectic side (tests of personality, as they are sometimes called—in a somewhat narrower sense) are far less effective, and call for a fuller discussion.

(a) First, there are tests depending on the method of *expression*, such as the psychogalvanic reaction, the measurement of pulse-rate, rate of breathing, blood pressure, unconscious movement and the like. All except the first prove to be of very little value as indications of emotional disposition. Biochemical tests and some of the newer tests for the reactions of the autonomic system are more promising; but the determinations require a good deal of time from a highly skilled specialist, and have a decidedly low reliability.

Recently several workers have re-investigated what they call " objective " tests for personality, i.e., tests which (unlike the more popular " projection " tests) involve no subjective element in the marking; and high claims have been put forward. The evidence most frequently cited is their proved capacity to discriminate significantly between groups of normals and of neurotics or different types of neurotic. However, group discrimination is no guarantee of individual discrimination ; and in my own experiments the great defect of the test-results has been the way they vary from one occasion to another with the mood or fitness of the examinee—a point on which their advocates give only meagre information.*

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* To save detailed descriptions, I name only the more common and conspicuous traits.

In principle one might expect tests of expressive actions to give far better results. Early trials with June Downey's handwriting tests, and attempts to assess the speed, frequency, strength, extent, and variability of the movements made in walking, drawing, speaking, gesticulating, reacting with the facial muscles, and the like, seemed at first decidedly promising. Nevertheless, more recent investigations indicate that the reliability and validity of the results are not so good as those of subjective or impressionistic judgments based on direct observation of facial expression and expressive movements generally, provided the observer himself has been adequately trained.

(b) Tests depending on some method of *impression* yield far better results. The best appear to be those depending on free association, apperception of blots or ambiguous pictures, preferences for pictures (shown by ranking), and completion tests designed to reveal the examinee's emotional attitudes by getting him to complete a story or criticize imaginary characters. The old apperception tests, renamed projection tests (a title which, as a recent critic has said, rests on good salesmanship but bad psychology), have of late become fashionable. But their value has been much over-rated, partly because their advocates so seldom support their claims with adequate validation-data. A review of what figures are available suggests that in general the reliability of such methods is only two-thirds, and the validity less than one half, that ordinarily reached with tests of cognitive abilities and attainments.

Yet critically employed they undoubtedly form useful accessories. First, they are of considerable assistance where a large number of cases require a rapid preliminary screening. Secondly, they help to standardize assessments submitted by different investigators. Thirdly, they provide tactful routine methods for eliciting points of departure which can be fruitfully followed up during a personal interview. Of the tests given orally and individually, the ranking and interpretation of pictures and the Rorschach blot test (marked for content rather than for the characteristics on which Rorschach and his followers chiefly rely) are among the most serviceable. Of the written procedures, the camouflaged questionnaire (which can be scored as a test) is, as we shall see in a moment, by far the most informative.

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* At the Maudsley Hospital, Dr. Clarke and Dr. Gravely have recently made careful studies of tests of a motor type (muscular tension, static ataxia, body-sway in response to suggestion, motor disturbance during association tests, e.g., the Luria technique, etc.) and of a sensory type (flicker, dark adaptation, autokinetic illusion, fluctuation of ambiguous figures). Their general conclusion is that, although there are usually positive correlations, the size of the correlations is too low for the needs of practical diagnosis : (Clarke, A. D. B., " Measurement of Emotional Stability by Means of Objective Tests," *Brit. J. Educ. Psychol.*, **20**, 1950, p. 202 ; Gravely, A. M., " Perceptual Tests as Measures of Temperament," *ibid.*, p. 203). With such tests the discrimination between groups is of about the same order as the discrimination between mentally defective children and normals on the basis of height : with sufficiently large samples (50 of each) the group-difference in average height is " statistically significant." But the non-statistical reader is apt to interpret the phrase " significant discrimination " to mean much more than this.

With children it is desirable to distinguish, whenever possible, between what is innate (i.e., attributable to the child's genetic constitution) and what is acquired. No measurement obtained direct from a test, not even the I.Q.'s obtained from an intelligence test, can be relied upon to do this just as it stands. But, when interpreted and perhaps corrected in the light of other information (e.g., details regarding the family history), a fairly trustworthy assessment of the two hypothetical components can often be secured in the case of such tendencies as general emotional instability and certain instincts, like sex, anger, fear, or gregariousness).*

In the cognitive field, tests for general ability and for special aptitudes have largely been developed on the basis of some theory of the structure of the mind, usually a factorial theory ; but in the field of orectic psychology most of the well known tests have generally been put forward without any such theoretical basis, or with a basis that is popular rather than scientific (e.g., such assumptions as "preference for colour indicates emotionality," "attention to dark shading a melancholy disposition," etc.). Instead of saying : "here is an important and verifiable component, how can it be tested?," the inventors seem usually to ask : "here is an ingenious idea for a test : what plausible inferences can I draw from the responses ? " As a result, the interpretations one encounters, even in accredited journals, appear to rest more on analogies and symbolisms of the brand found in the mediaeval dream-book than on a scientific knowledge of mental processes. A common excuse is that each personality is unique, and therefore the test-responses must be interpreted as wholes. But analysis does not preclude a subsequent synthesis ; indeed, the synthesis is likely to be far more trustworthy if it rests on a sound analytic procedure.

2. *Questionnaires and rating scales.*—The questionnaire occupies a position midway between the more formal tests and procedures based on subjective observation. It is regularly used in most American hospitals and clinics. With adults considerable reliance is placed on answers written by the patient himself ; and too often their manifest content (to borrow a Freudian phrase) is accepted at its face value. But the validity of the results depends largely on the examinee's motivation and general attitude towards such interrogations. An applicant for a responsible post, or a delinquent whose peccadilloes have come under criticism, can hardly be expected to convict himself ; on the other hand, a member of the forces hoping for discharge may frankly admit his

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* This lecture was delivered in 1951 ; and it is encouraging to note that, in later publications, writers like Professor Vernon, Professor Cattell, and Dr. Eysenck have expressed very similar views about the more popular types of "personality test." In a valuable review, published since the above was written, Professor Vernon observes that, in his opinion, "the attempt to measure inborn factors is misguided . . . We can never separate what is innate from what is acquired ; even if we could test the former, it would scarcely help us in the practical problems of predicting behaviour" (*Personality Tests and Assessments*, 1953, pp. 81–2). But his book has chiefly in view "the field of selection," which he regards as "the most straightforward" ; it "does not deal specifically with the diagnosis of abnormal personalities." Consequently he relies for his evidence largely on results obtained in allocating adults to specific occupations (notably in the forces). In such cases the distinction between what is innate and what is acquired is undoubtedly of little value, and the requisite evidence would be difficult to procure. But with boys and girls of school or pre-school age, studied intensively at a child guidance clinic, the distinction is easier, though still hypothetical.

weaknesses and even exaggerate them.* Quite apart from conscious reticence, no patient can be expected to be explicitly aware of what is irrational or peculiar in his own feelings and behaviour. Moreover, in this country, class-differences may greatly alter the implications of the replies.†

To a large extent these sources of error can be avoided by camouflaging the purpose of each item; and those who interpret or criticize the results must remember that their significance is to be judged, not by what the patient is trying to convey, but by the empirical correlations already discovered between this or that kind of reply and this or that type of personality. I have attempted to draw up such a questionnaire for use in this country. The total score (on the 100 selected items) may be taken as representing general emotional instability; but in addition, the classification of symptoms enables a " profile " to be drawn up for more specific tendencies (anxiety-neurosis, hysteria, neurasthenia, etc.). It is indeed the pattern of group-scores rather than any single set of marks or measurements that is most revealing.‡ Several of the more recent American questionnaires claim to measure distinct traits or distinct types of neurotic tendency. The critics commonly object that the separate measurements are all too closely correlated to be accepted as indicative of separate characteristics. But the answer is that the general factor of emotionality enters into all; and this must be allowed for in judging the resultant pattern. With badly constructed questionnaires the general factor may largely represent the different attitudes or degrees of candour shown by those who reply. In any case it is unwise to accept the classificatory claims made for inventories and questionnaires unless they have been checked for factor analysis (see, for example, the factorizations, made by Banks, Keir, Flanagan, and Mosier, of the well known scales and inventories constructed by Bernreuter and others: Banks, C., & Keir, G., *Brit. J. Psychol. Stat. Sect.*, V, 1952, pp. 19–31 and refs.).

With children the questionnaires and rating scales are generally intended for the use, not of the patients, but of those who know them, particularly their teachers. But the contents should be as factual as possible. As was demontrated in an early experiment§, a teacher's judgments are likely to be far more accurate if the questions submitted to him relate to observed instances of behaviour, not to impressionistic assessments of abstract qualities. Afterwards the investigator can, if he wishes, group the replies according to some scheme of abstract qualities or traits ; but there must be prior evidence for the inferences proposed.

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* These differences in motivation no doubt largely account for the widely discrepant figures published by various investigators for the reliability and validity of such procedures. Thus, A. Ellis (" The Validity of Personality Questionnaires," *Psychol. Bull.*, **40**, 1946, pp. 385–440) finds that, out of about 400 investigations, the validating correlations were less than 0·40 in very nearly one half the inquiries: of the better known questionnaires, the Minnesota Multiphasic Inventory appeared the most efficient; the Woodworth, the Thurstone, and the Bernreuter among the least. On the other hand, those who have summarized work in the U.S. Forces have reported much more favourably (cf. D. H. Harris, " Questionnaire and Interview in Neuropsychiatric Screening," *J. Appl. Psychol.*, **30**, 1946, pp. 644–48, and S. A. Star ap. S. A. Stouffer, *et al.*, *Studies in Social Psychology in World War II*, Vol. **4**, *Measurement and Prediction*, 1950).

† In experiments which I carried out for the Institute of Industrial Psychology, I found that the scores for neuroticism obtained in some of the American questionnaires by comparatively stable teachers and undergraduates (especially those of a self-analytic type like students taking first-class honours in Arts) are much higher than those obtained by highly neurotic business men or skilled artisans. Thus the scores must be separately validated, not only for the two sexes, but also for different social classes. With those whose educational level or type of work makes the filling up of written forms a somewhat repugnant task, far better results can be obtained if the questions are typed on cards, and dealt in separate trays for " yes " and " no."

‡ *The Subnormal Mind*, 1935, Appendix III, pp. 361 f.

§ *Brit. Ass. Ann. Rep.*, 1915, *loc. cit. sup.*

As with tests so with questionnaires, it is always important to know how far results agree when the same procedure is employed with the same group of children on two or more successive occasions. In nearly all such inquiries the " reliability coefficient " (which measures this type of consistency) proves to be far from perfect. Hence it is a sound principle to base one's final judgments, not merely on a representative sample of reactions, noted on a single occasion, but also on a representative sample of occasions. Assessments expressed in terms of a prescribed rating-scale are usually most accurate when derived by a process of ranking (ties being freely allowed) ; when only one person is to be observed, the characteristics may be ranked for the person instead of ranking the persons for the various characteristics ; this provides a useful check on the attempt to allot ratings by absolute impression.

One advantage that questionnaires and rating-scales possess over experimental tests is obvious. It is far easier for those who construct such devices to select questions which relate directly to the more important aspects or components of personality.* Further, unlike tests, questionnaires can be made to throw light on the *interactions* between different traits or tendencies. Two or more children, for example, may have equally high assessments for " Sex " and " Submissiveness " ; but, when such tendencies are aroused simultaneously, each child may try to solve the ensuing conflict in very different ways. Let me add that a stock questionnaire, even if it is not filled up in writing for each individual case, may be useful as a guide or reminder to the psychologist, and help to render his own judgments more complete and more objective.

3. *Interviews.*—The value of the interview has been severely criticized ; nevertheless it is impossible to dispense with it. It is true that of late a number of psychologists, and (surprisingly enough) even some psychiatrists, have extolled the superior merits of what they style " diagnostic " tests, as though a diagnosis could be based on test-results alone. Yet even in cases of alleged mental deficiency, where tests are more trustworthy than for any other condition, no one should pronounce a diagnostic verdict without also making a personal investigation of the patient and his history.

Of all the techniques available, the interview is the most comprehensive. It covers far more ground in far less time, and without the need for special materials or specialized standardized devices. It can be quite elastic: the examiner can break off the line he is following at any moment if it is proving fruitless and embarrassing; he can follow up new points as they arise, and explore new problems as they present themselves. Indeed, in the broadest sense of the word, the interview can be stretched to include most of the other devices, while at the same time it permits observations of a kind that could not be secured by any other means. For example, it is impossible to reach a satisfactory estimate of a person's mental traits without also considering his physical characteristics; and these can only be judged by direct observation. At the same time it is perhaps necessary to remind the physician that the physical examination will only form a minor part of the procedure: there are still a number of practitioners who attempt to base their conclusions on a purely neurological examination together with an inspection of so-called stigmata and body-build. Careful research has shown that the inferences commonly drawn from body-build and the presence of stigmata are not without a certain element of truth; the correlations between such characteristics and the mental qualities they are supposed to indicate are nearly always positive; but they are far too low to be of much practical value by themselves.

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* In spite of this the majority of questionnaires seem to have been constructed without any clear rational basis. A few have been drawn up with some theory of personality-structure in mind, e.g., those which contain lists of questions about situations and responses corresponding to the main human instincts or about the examinee's acquired attitudes and interests. Others, like Humm and Wadsworth's " temperament scale," are framed on the assumption that the essential characteristics of any individual person can be described in terms of certain " components," which, when extreme, are manifested as definite disorders—the hysteroid, paranoid, epileptoid, schizoid, manic-cycloid, depressive-cycloid, and the like. Murray's thematic apperception test is founded on a scheme of " needs " and " presses " : but these were suggested chiefly by psychoanalytic speculations, not by any verified theory of personality-structure.

Yet, in spite of its apparent advantages and the wide opportunities which the interview affords, the published results give surprisingly low figures for its reliability and validity. Two psychiatrists examining the same patients in ignorance of each other's findings will, as a rule, disagree over their diagnoses in nearly 50 per cent. of the cases. Measured by a coefficient of correlation, the "reliability" (i.e., consistency) of two independent interviews ranges as a rule from 0·4 to 0·6—figures that would tempt a psychologist to reject any new test forthwith, if it were intended to measure cognitive ability. The "validity" of the results secured by such procedures is lower still: if we can trust the coefficients generally reported, it seldom rises even to 0·4.*

With figures like these it is scarcely surprising that many psychologists have been inclined to dismiss the interview as altogether too subjective. In my opinion, however, the fault lies not so much with the interview as such, but with the untrustworthy methods commonly employed, and the notions on which those methods rest. As a rule the interviewer's procedure is far too casual and sorely in need of further refinement. Carried out in the customary fashion, the average interview may admittedly furnish results that are devoid of any scientific value. If, however, we restrict our comparison to conclusions reached, not by the ordinary untrained interviewer, but by observers who base their procedure on a sound knowledge of psychology, and who know what devices can be trusted, which traits effectively assessed, and what are their own special weaknesses, then we shall find that their judgments may claim an accuracy and a diagnostic value far superior to those of any test or questionnaire.

4. *Standardized situations.*—Nevertheless, even at its best, the interview, like the test, suffers from one manifest and unavoidable drawback. Of necessity it involves a restricted, unusual, and distinctly artificial situation. It is

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* Cf., for example, Ash, P., "The Reliability of Psychiatric Diagnoses," *J. Abn. Soc. Psychol.*, **44**, 1949, pp. 272 f.; Stouffer, *loc. cit. sup*, pp. 475 f.

therefore necessary to supplement it by special expedients. With a little stage-management it is possible for the psychologist or social worker to study the children referred to him under conditions which resemble everyday occurrences and are yet more or less standardized so as to be the same for all. Under cover of a tea-party, or a visit to some place of interest (the Zoo, a museum, a cinema, or a pantomime), or a ramble in the park with incidental games, he can set a series of practical problems to be solved by the children themselves, allowing each youngster sufficient latitude to exhibit his or her natural proclivities, whether of enterprise or leadership, timidity or bad temper, or preference for the opposite sex. With a playroom, and suitable toys and models, much the same kind of situations can be achieved or imitated even on the premises of the clinic. Records of individual behaviour can be entered up on a previously prepared schedule ; and these can be made to furnish material not only for specific ratings and assessments, but also for a synoptic portrait of the child's general character. The use of such standardized situations affords one of the most fruitful means of studying individual cases. But once again the details of the procedure must be systematically planned beforehand in the light of an acceptable theory of personality.*

CONCLUSION.

It is difficult to sum up in brief terms the relative efficacy of the different methods I have described. The figures reported in the literature vary so much according to the type of persons investigated, the experience of the investigator, and above all the nature of the particular characteristics assessed, that generalizations are bound to be precarious. On the whole, it may be said, within their somewhat limited range, the best assessments are those derived from standardized real-life situations of the type just mentioned. Next to these, and of far wider scope, come assessments based on interviews carried out by trained interviewers using refined techniques. Of the more mechanical devices the camouflaged questionnaire appears to be the most satisfactory. The formal and so-called " objective " tests are far less trustworthy, except as regards cognitive abilities and intellectual attainments.†

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* Recurrent real life situations were exploited in this way for the early studies cited above (*Brit. Ass. Ann. Rep.*, *loc. cit.*) ; and standardized situations in the playroom, etc., were, I believe, first regularly used in our early studies with juvenile delinquents. (*The Young Delinquent*, 1925, pp. 418 f., and *Character and Personality*, **7**, 1939, pp. 238–54, 285–99). With adults somewhat similar devices were used by War Office Selection Boards during the recent war and the Civil Service Selection Board after the war.

I may add that, with children, I have usually warned parents or teachers proposing to bring children to the psychological clinic not to say anything about the real purpose of the visit. It then becomes possible to prevent the child, at any rate during the early stages of the first interview, from knowing who the interviewer really is : he can be left to suppose that a friendly stranger is just amusing him with pictures, toys, and a few harmless questions, while mother or teacher is having a serious talk about her special problems somewhere else. This way of breaking the ice will generally circumvent the secret dread which nearly every youngster experiences when face to face with a " doctor " who (so he gathers) is " going to test his brains." The more natural the whole situation can be made to appear to the patient or examinee, the more reliable will be the results.

† The foregoing inferences and the conclusions that follow are based mainly on a series of investigations reported in an earlier article on " The Assessment of Personality " (*Brit. J. Educ. Psychol.* **15**, 1945, pp. 107–21), supplemented by the results of more recent researches.

For the practical worker the most important inference, I fancy, is this. In assessing personality the ideal procedure will, as a rule, consist of an eclectic combination of all the different methods, not of a single method only. Thus both the mode of approach and the separate assessments will be composite. In the cognitive field, it may be remembered, as soon as this basic principle was grasped, rapid progress was made. At the outset of the present century, pronouncements about the value of mental testing had become increasingly unfavourable ; but nearly all the earlier investigators had assumed that the ideal to be achieved was a single specific test for each particular trait. Later the results of factorial analysis disclosed both the possibility and the value of working with composite resultants ; and Binet convincingly showed how even such a fundamental trait as general intelligence could best be assessed by means of a heterogeneous scale, composed of a wide variety of test-items. What holds of general intelligence holds still more strongly of other characteristics of human personality ; and it is manifestly true of each personality viewed as a whole.

Thus the final case-summary should comprise, not merely analytic assessments in quantitative terms of the chief key-tendencies or "factors," but also a synthetic character-sketch, giving a qualitative picture of the individual, viewed as a dynamic, integrated, and unique human being. The plan of examination, and the terminology by which the results are described, should be based, not on some plausible but untested theory, improvised by the investigator, or suggested by the speculations of whatever school has excited his interest ; they should rest on an eclectic foundation, common to all competent workers in the same field. And that in turn can only be effectively built up by starting from established views on the general nature of human personality, as set forth by authoritative psychologists and verified by the aid of experimental and statistical research. Since after all there is so much, even in the best of current doctrines, that still awaits confirmation, the final moral is the need for further scientific research.

SCHIZOPHRENIA: A NEW APPROACH. II. RESULT OF A YEAR'S RESEARCH.*

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About one year ago, with the encouragement of the Editor-in-Chief, a short paper appeared in this Journal entitled "Schizophrenia; A New Approach" (18). In this paper it was noted that mescaline and adrenaline have a similar biochemical structure. It was suggested that one of the aetiological agents in schizophrenia might be a substance or substances lying between these two; with the psychological properties of mescaline but effective in concentrations nearer those of adrenaline. Dr. Harley Mason elaborated this suggestion from the biochemical standpoint. For convenience these hypothetical substances were called, collectively, M substance. If M substance occurred in the body, it would account for the group of illnesses usually referred to as schizophrenia better than any hypothesis so far advanced. It has been the good fortune of the co-authors of that first paper (J. R. S. and H. O.) to be able to join forces with the third author of this paper (A. H.) to test the hypothsis. It is with the efforts of the last year that this paper is concerned.

A proposition such as this sounds simple enough to test when sketched on paper, but once it is tackled in the laboratory and the ward, many difficulties soon appear. Money must be obtained, technical help sought, workers from other disciplines must be persuaded to give their support. When all this has been achieved, and it is no small achievement, one has not even started. First of all one must decide where to start. In the range of substances which lie between mescaline and adrenaline there are many hundreds perhaps thousands of compounds. Some of these have been made and are well known to pharmacologists, but many have found no place in medicine and are hidden away in obscure corners of the literature, or having no effect on a particular experimental animal have never been recorded in print. To make or obtain such a large number of compounds would be costly and laborious, but this work and expense would be but a tithe of the effort required to test them. For, since animals are unable to talk and so inform us of their experiences, testing must always be done on human volunteers.

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So, a year ago, although we had received the keenest support from the Director of Psychiatric Services of the Provincial Department of Public Health, Regina, and although the Federal Department of Health and Welfare in Ottawa had secured a most generous grant for us from Dominion funds, putting us in a position to start work, there remained an unanswered question, "Where do we start?"

In order to answer this question an extensive survey of the literature was made in greater detail than had been possible for the first paper. We paid special attention to the chemistry and pharmacology of substances known to produce disturbances in perception, feeling, thought and behaviour without marked changes of consciousness. This survey showed that both Lindeman (13) and de Jong (11) had been aware that a chemical relationship existed between mescalin and adrenalin, but neither of them had linked this with Cannon's conception of stress, nor did they suggest that it might have special importance.

De Jong had, in order it appears to be "objective," made his jumping off place the occurence of catatonia in small mammals and discovered that if large doses are given an almost unlimited number of substances can cause catatonia. He paid little attention to whether the catatonia was produced by large or small doses, or whether the substances themselves were likely to occur in the animal body. His findings were, therefore, unlikely to be of much assistance to those engaged upon a research into schizophrenia which is remarkable for being accompanied by few clearly demonstrable biochemical, anatomical or electrophysiological changes even when the psychological disturbances are most disastrous.

We, therefore, limited our enquiry to substances which could produce psychological disturbances similar to those found in schizophrenia without causing clouding of consciousness, confusion, or gross physiological disturbances.

Hallucinogens.

As a working hypothesis we supposed that M substance was chemically closely related to adrenalin. This enabled us to narrow the search from hundreds of potential M substances to those lying on a continuum between mescalin and adrenalin. However, it was possible that the similarity in chemical structure between mescaline and adrenaline was purely due to chance. In order to test this inference we searched the literature to determine whether other compounds were able to produce psychological disturbances similar to mescaline and had a similar chemical structure.

When the literature is examined to catalogue these hallucinatory substances, which for convenience we have called the hallucinogens,* one is struck by their small number. Those that will produce their effects without being accompanied by other disturbing symptoms can easily be counted on the fingers of two hands and those whose chemical structure is known on the fingers of one hand.

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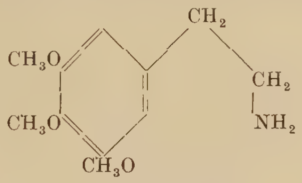
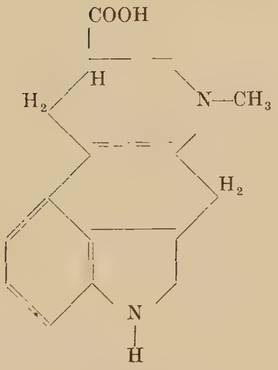
* One must always offer some excuse for coining a long new word, but there is really no other satisfactory one. It is not a good word but seems to us less obscure than eideticum or phantasticum and begs the question less than "schizogen" or "schizophrenogen." As Klüver has observed when we take these remarkable compounds we enter a world beyond language, so it is hardly surprising that they may be difficult to name.

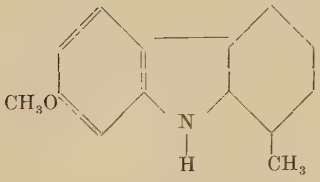
We have so far obtained some information on five compounds which may be called the hallucinogens: mescaline, lysergic acid diethylamide, harmine, ibogaine and hashish. The active hallucinogenic principal in hashish has not yet been definitely established. The structure of the other compounds are shown below, with exception of ibogaine which is known to have an indole nucleus and is placed among the indole alkaloids, Mankse and Holmes (14).



Mescaline.



Lysergic acid.



Harmine.

Fig. 1.

These then are a group of compounds that have an indole nucleus in common, assuming that in mescaline the side chain can readily be fused by its amino group to form an indole compound. It might, therefore, be that the indole ring is associated with hallucinogenic properties, provided the compound is able to cross the blood brain barrier. This in itself did not bring us any closer to M substance since these compounds are all plant alkaloids and are unlikely to be present in the body.

Pink Adrenaline.

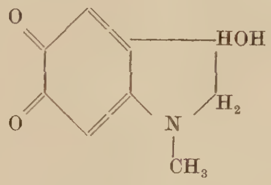
Shortly after we completed our first paper an observation was made by one of us (J. S.) in curious circumstances. In the hopes of interesting a young and brilliant historian in our work so that he could be persuaded to take mescaline, he was invited to listen to a recording of a recent mescaline experience of H. O.'s As the recording continued it became evident that the interest and curiosity which it had at first evoked was soon replaced by anxiety and alarm. At last the historian remarked " I have also had such things happen to me." He then explained that for many years he had suffered from asthma, and that when he had a severe attack he would become " an adrenaline addict." He had experienced eidetic and hypnagogic imagery since childhood and had found that these large doses of adrenaline increased this imagery to an alarming extent and when his eyes were open " things looked different."

This valuable piece of information combined with a careful scrutiny of adrenaline and its near neighbours suggested that if adrenaline could be deprived of its pressor qualities it might itself be a hallucinogen. A search was then started among people taking adrenaline medicinally to see if they had similar experiences. We have discovered several. A young woman, asthmatic since she was seven, was controlled only by large doses of adrenaline. At the height of her adrenaline consumption she would have visual hallucinations of faces floating across the ceiling. These she related to the adrenaline injections and so did not endow them with any affect. Another woman with urticaria became frankly schizophrenic shortly after receiving an injection of adrenaline to control her allergic condition. The experience was of short duration. Another volunteer, who had the previous day taken lysergic acid diethylamide, was discussing his subjective impressions. He then volunteered that as a boy he had controlled his asthma by means of adrenaline sprays. Often after these sprays he had been aware of subjective changes very similar to this lysergic acid experience. Finally a young medical student reported that after receiving adrenaline to control his asthma he lost much of his ability to empathize ; for instance, when driving, he is normally sensitive to the presence of children on the road who might be harmed. After adrenaline injection there was a tendency to allow the children to shift for themselves. Lindemann (13) showed that adrenaline injections markedly aggravated the symptoms of half the schizophrenic patients he studied.

At this point we were lucky enough to obtain another clue from Dr. Asquith, anaesthetist at the Regina Central Hospital, who told one of us that when he was in England during the late war he had been forced, owing to shortage of supplies, to use adrenaline solution which was somewhat deteriorated. Anaesthetists discovered that, if much larger doses were injected than usual, pressor effects similar to those of the fresh solution could usually be obtained. This was thought to be satisfactory until it was noticed that there were more unfavourable " reactions " than with the fresh solution. It appears that some of these reactions were psychological disturbances, sometimes of an alarming sort. No special study of these psychological upsets were made because they were transient and it was considered necessary to avoid them rather than to investigate them. However, Asquith's observation drew our attention to "pink adrenaline."

At our first meeting in Saskatoon with our colleagues in the research, Professors Hutcheon, MacArthur and Woodford, we raised the question of "pink adrenaline" and put forward a suggestion about its composition. Hutcheon pointed out that "pink adrenaline" certainly contained among other things adrenochrome. In the exciting ten minute discussion which followed after Hutcheon drew the spatial formula of adrenochrome, it was shown that this substance was related chemically to every hallucinogen whose chemical composition has been determined.

The structure of adrenochrome is :



It is evident that we had stumbled upon a compound which has an indole nucleus in common with the hallucinogens, which is readily derived from adrenaline in the body, and which can be fitted into a logical scheme relating to stress. Under stress the quantity of adrenalin in the body will increase and this might be turned into adrenochrome in the schizophrenic individual.

Hutcheon agreed to synthesize and determine the toxicity of adrenochrome without delay. All our studies have been made with this synthetic adrenochrome.

It should be noted that adrenochrome, which is very unstable, is not the only substance which would be present in a decomposing solution of adrenaline. Such a solution could contain numerous degradation products of noradrenaline and adrenaline. This is the uncertain mixture that was given to patients who had been anaesthetized and possibly injected with morphine and atropine derivatives. Unfortunately, no study was made of these reactions so we can only speculate about the numerous possibilities.

Adrenochrome.

This substance was discovered in 1937 by Green and Richter (10) who found that it played a role as an hydrogen carrier in concentrations that fall within the physiological range . It was found in skeletal muscle in a concentration of about 1×10^{-7} moles. There is still some doubt whether adrenochrome is present in the body. Beyer (4) completely ignores adrenochrome. However, Bacq (2) states "adrenochrome and its derivitives are certainly the most interesting oxidized derivatives of adrenaline. It is an error to consider adrenochrome as an inactive substance because it has completely lost its classical sympathomimetic action." Martin (15) states that adrenochrome is pharmacologically inactive but it is biochemically active.

There are three important bits of evidence for the presence of adrenochrome in the body: (1) Adrenochrome and its oxime (adrenoxyl) form excellent haemostatic substances and have been used therapeutically as vitamin P factors. They increase capillary resistance as well. When adrenaline is injected into a rabbit haemostatic activity appears after four minutes, is maximal after seven minutes and lasts for hours. Adrenochrome injection produces maximum haemostatic activity after three minutes. This is then evidence that the oxidized product of adrenaline may be the hemostatic agent, not adrenaline itself. (2) Adrenochrome being a quinone possesses many properties of the quinones. It oxidises sulfhydril groups of glutathione, proteins and enzymes and thus is able to inhibit the activity of many enzymes of the glycolytic cycle, Meyerhoff and Randall (17) and the enzymes of the tricarboxylic acid cycle, Woodford (20). It has thus been found that adrenochrome inhibits the mitotic rate of growing cells probably because it interferes with the glycolytic cycle, Lettre (12). Bullough (6) found that, when mice were stressed by overcrowding, the adrenal medulla increased in size by 80 per cent. while the cortex increased 30 per cent. The epidermal mitotic rate fell 60 per cent. They also reported that *in vitro* adrenaline was not an antimitotic agent but that *in vivo* it was, whereas adrenochrome was antimitotic both *in vitro* and *in vivo*. They concluded that the antimitotic factor in the stressed mice was adrenochrome. (3) Martin, Ichniowski, Wisnasky and Ansbacher (16) found that para-amino-benzoic acid inhibited the action of tyrosinase on adrenaline and this vitamin should, therefore, increase the sympathetic effect of adrenaline by blocking its conversion to adrenochrome. When administered to dogs it did increase their blood pressure and caused mild hyperglycaemia. This provides evidence that phenolases are active in the *in vivo* destruction of adrenaline.

There are at least five important ways, Bacq (2), in which the body detoxifies the rather large quantities of adrenaline that are produced by the adrenal medulla and the other sympathetic ganglia. These are:

(1) by excretion unchanged in the urine;
(2) by storage of active adrenaline within the cells;
(3) by deamination of the side chain to form oxidizable aldehydes;
(4) by esterification of the phenolic hydroxyls;
(5) by quinone formation to adrenochrome and its derivatives.

The deamination is catalysed by the enzyme amine oxidase; the esterification is catalysed by the enzyme sulfoesterase; and the quinone formation is catalyzed by the enzyme phenolase. Of the three main detoxification mechanisms amine oxidase forms compounds with no autonomic properties and which are easily metabolized. Sulfoesterase forms inactive adrenaline esters and these are so excreted in the urine. Phenolase forms adrenochrome which has no pressor properties but does have other important effects. If therefore one blocks either amine oxidase or sulfoesterase the adrenaline may be diverted into adrenochrome.

Substances that block amine oxidase should, therefore, divert adrenaline into adrenochrome formation. Amine oxidase is present chiefly in the liver, intestine and central nervous system and converts adrenaline into 3, 4-di-hydroxyphenylhydroxyacetaldehyde. Burn (7) believes that amine oxidase plays a role in the sympathetic nervous system comparable to acetylcholine esterase in the parasympathetic system. The enzyme has been found around the sympathetic nerve endings in blood-vessels, the nictitating membrane and the iris of the cat. It destroys noradrenalin more quickly than adrenaline. Blaschko (5) made the interesting observation that compounds having the structure R—C—CH_2—NH—CH_3 were inhibitors of amine oxidase. These findings have been supported by Beyer (3) who reported that phenylpropylamines having the amino groups on the terminal carbon were oxidized by amine oxidase, but that, if the hydroxyl groups were present on the ring, the compounds was oxidized by phenolase. If the benzene ring contained no hydroxyl and, if the amino group were on the carbon adjacent to the terminal carbon, neither enzyme could oxidise it. The following compounds contain the grouping found to inhibit amino oxidase ; cocaine, ephedrine, indole, indoleacetic acid, phenylisopropylamine, desoxyephedrine, pervitin, benzedrine, oxidized derivatives of adrenaline (adrenochrome), caffeine, nicotine, methedrine, and lysergic acid.

Electroencephalographic and other Studies of Adrenochrome.

Woodford's (20) studies have shown that when adrenochrome gets into the cerebral cells it inhibits markedly intermediary metabolism of carbohydrates. Eade and Hutcheon's (8) studies on the lowering of body temperature by adrenochrome at the same time as body metabolism is increased, indicates that adrenochrome lowers body temperature by some central effect. This is suggestive evidence that adrenochrome can cross the blood brain barrier in contrast to adrenaline which is not able to do so. To test this possibility further intravenous adrenochrome was given to a series of volunteers (normals and patients) and E.E.G. records were taken on some. In epileptics with definite cerebral dysrhythmias the adrenochrome markedly increased the generalized arrhythmia within half an hour. The focal activity became more prominent. In people with a normal E.E.G. and a clinical history of epilepsy the adrenochrome clearly brought out the epileptic activity within half an hour better than metrazol does. In one schizophrenic subject the E.E.G. showed much dysrhythmia after adrenochrome whereas it was essentially normal before. A typical record before and after adrenochrome is shown below, Szatmari (19). This is further evidence that adrenochrome can rapidly cross the blood brain barrier and interfere with the oxidative processes of the cerebral cells. Further experiments are being made in animals with radioactive adrenochrome in order more definitely to localize the site of action of the adrenochrome.

We are now using adrenochrome as a routine in establishing the diagnosis of epilepsy since it so clearly brings out the epileptic activity. We believe that this is the first time a substance thought to be present in the body has been shown to effect the E.E.G. so markedly. The implications regarding epilepsy are being explored by our research unit.

Effect of Adrenochrome on Cerebral Respiration.

It has been shown that adrenochrome inhibits hexokinase (17) under anaerobic conditions. Naturally this would inhibit the entire oxidative system starting with glucose. Woodford (20) in confirmation reported that adreno-

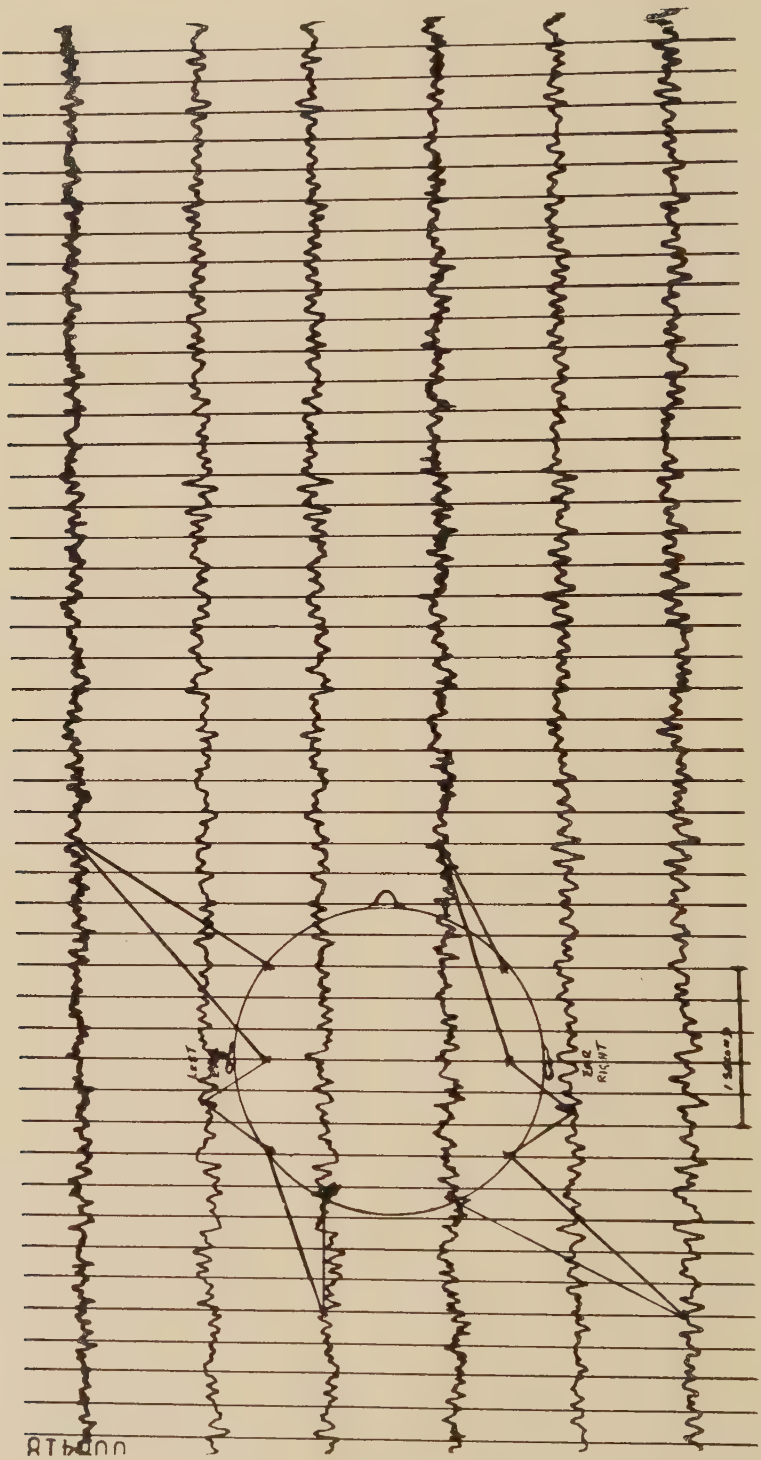

LEFT EAR
EAR RIGHT
1 SECOND

FIG. 2.—(*a*) Epileptic subject interseizure pattern.

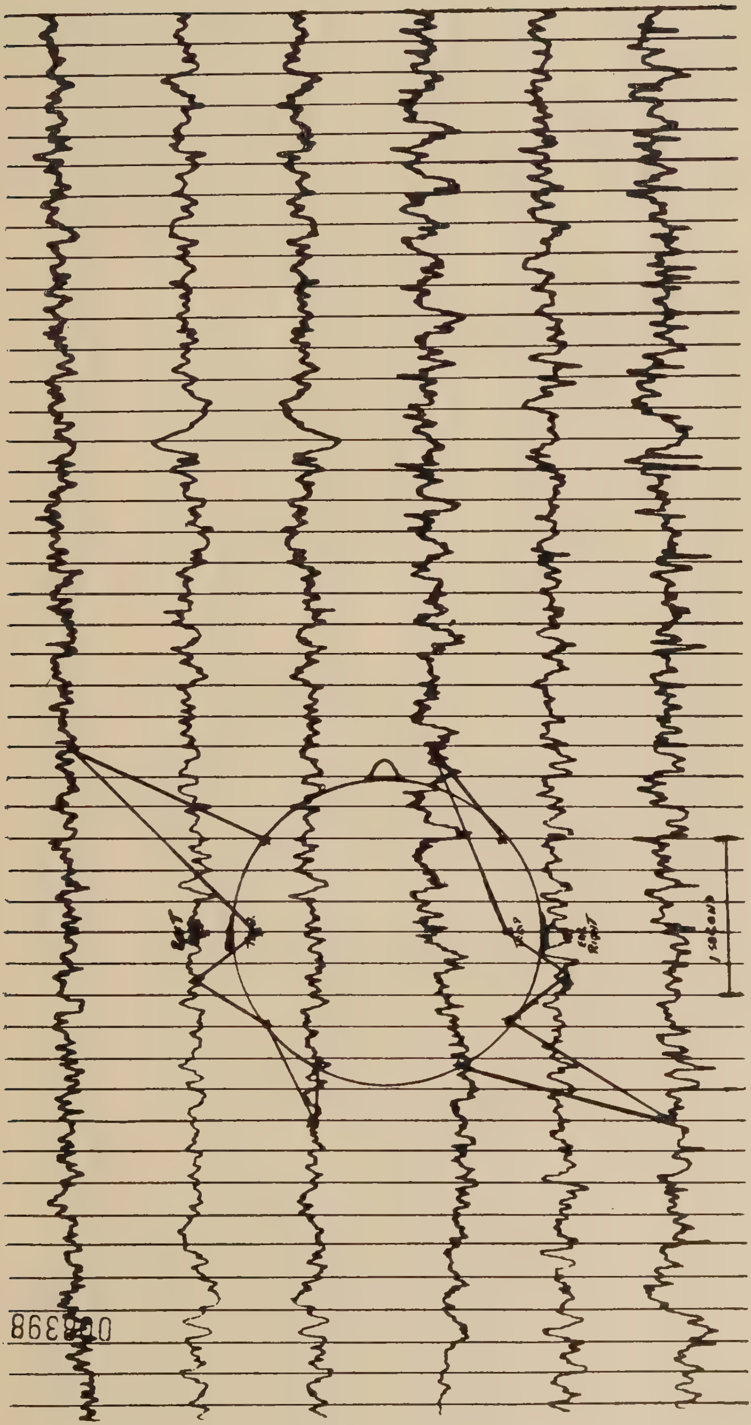


FIG. 2.—(*b*) Same E.E.G. run 45 minutes after 10 mg. of adrenochrome (intravenous).

chrome inhibited oxidation by brain tissue immediately upon addition to the system under aerobic conditions. Woodford (20) found that adrenochrome, in contrast to mescaline which requires a two to three hour preliminary incubation period with the brain tissue before consistent inhibitory results are obtained, shows inhibition immediately. Since the aerobic oxidation of both glucose and pyruvate is inhibited by adrenochrome, he interprets this as meaning that, in addition to hexokinase inhibition, an enzyme occuring below the pyruvate level is also blocked.

Some Pharmacological Experiments with Adrenochrome.

Eade and Hutcheon (8) found that the LD_{50} of adrenochrome to be 137 mgm. per kg. Signs of intoxication included progressive paralysis of the hind limbs, dyspnoea, apathy and exophthalmia. They further found that adrenochrome has a hypothermic action in normal and adrenalectomized rats.

Some Psychological Effects of Adrenochrome.

Once the toxicity of adrenochrome had been established in animals it was possible to begin trials in humans. It was uncertain how such an unstable substance should be given or what sort of dose would prove to have any psychological properties. On 9.x.52 two of us (A. H. and H. O.) therefore decided to start on ourselves using very small doses to begin with. Unfortunately, we later discovered that there was some doubt about the quantity of adrenochrome used in these first experiments because it was weighed out in a new and unfamiliar balance.

The first subject (A. H.) received what we supposed was ·1 mgm. in 1 c.c. of water subcutaneously. This makes a fine port-wine coloured liquid. The injection was accompanied by a sharp and persistent pain at the site of injection. There were no recognizable psychological changes. Blood pressure and pulse readings taken every five minutes for half an hour showed no change.

The second subject (H. O.) was given what we believed was 0·5 mgm. Again there were no pressor effects but there were marked psychological changes (see below).

Further experiments on our two wives and one of us (A. H.) using 1 mgm. subcutaneously produced some minor results, but by this time it seemed that our adrenochrome, which is very unstable, was beginning to deteriorate. On 16.x.52 5 mgm. of this deteriorating solution was given to H. O. and produced a response which was unpleasantly prolonged.

Since the subcutaneous injections were so painful, the first intravenous injection was given to a volunteer, Mr. C. R. Jillings, M.A., clinical psychologist. It was believed that adrenochrome given by this route would be much less painful. 1·0 mgm. of adrenochrome was, therefore, diluted with two 3 c.c. of sterile physiological saline and injected into the left antecubital vein. Almost immediately after the injection Jillings experienced a very severe pain which travelled up his left arm to the praecordium. This lasted about 10 minutes and was accompanied by pallor and sweating. There were no obvious psychological effects apart from alarm and dismay in the experimenters. It was later discovered that, if the adrenochrome solution is mixed with blood from the patient's vein, pain can usually be completely avoided.

Later A. H. and his wife both took 10 mgm. doses intravenously and had marked changes particularly in affect and behaviour. A. H. became overactive, showed poor judgment and lack of insight. R. H., his wife, became deeply depressed for four days and endured a condition which was indistinguishable from an endogenous depression. This unpleasant experience was aggravated by lack of insight, for she was unable to relate her depression to the injection of adrenochrome, although her change of mood came on immediately after it. An acute piece of observation by Dr. Roland Fischer, Ph.D. (9), suggests that this prolonged effect of adrenochrome was probably due to an attack of infectious hepatitis some years ago. It would therefore, be prudent to enquire about previous liver disease before injecting adrenochrome or other toxic substances into an experimental subject.

To those who are familiar with mescal and lysergic acid we would emphasize that judging from the little experience which we have, it does seem that adrenochrome is more insidious than these two hallucinogens, its effects last longer and possibly in consequence of this its administration is accompanied by a loss of insight. Since this may have serious results experimenters should guard their subjects very carefully.

Summary of an Account of an Adrenochrome Trial 9.*x*.52, 20-30 *hours approx.*
(Condensed from notes made at the time by the subject (H. O.).)

After the purple red liquid was injected into my right forearm I had a good deal of pain. I did not expect that we would get any results from a preliminary trial and so was not, as far as I can judge, in a state of heightened expectancy. The fact that my blood pressure did not rise suggests that I was not unduly tense. After about 10 minutes, while I was lying on a couch looking up at the ceiling, I found that it had changed colour. It seemed that the lighting had become brighter. I asked Abe and Neil if they had noticed anything, but they had not. I looked across the room and it seemed to have changed in some not easily definable way. I wondered if I could have suggested these things to myself. I closed my eyes and a brightly coloured pattern of dots appeared. The colours were not as brilliant as those which I have seen under mescal, but were of the same type. The patterns of dots gradually resolved themselves into fish-like shapes. I felt that I was at the bottom of the sea or in an aquarium among a shoal of brilliant fishes. At one moment I concluded that I was a sea anemone in this pool. Abe and Neil kept pestering me to tell them what was happening, which annoyed me. They brought me a Van Gogh self portrait to look at. I have never seen a picture so plastic and alive. Van Gogh gazed at me from the paper, crop headed, with hurt, mad eyes and seemed to be three dimensional. I felt that I could stroke the cloth of his coat and that he might turn around in his frame. Neil showed me the Rorschach cards. Their texture, their bas relief appearance, and the strange and amusing shapes which I had never before seen in the cards were extraordinary.

My experiences in the laboratory were, on the whole, pleasant but when I left I found the corridors outside sinister and unfriendly. I wondered what the cracks in the floor meant and why there were so many of them. Once we got out of doors the hospital buildings, which I know well, seemed sharp and unfamiliar. As we drove through the streets the houses appeared to have some special meaning. but I couldn't tell what it was. In one window I saw a lamp burning and I was astonished by its grace and brilliance. I drew my friends' attention to it but they were unimpressed.

We reached Abe's home where I felt cut off from people but not unhappy. I knew that I should be discussing the experience with Abe and his wife but could not be bothered to do so. I felt no special interest in our experiment and had no satisfaction at our success, although I told myself that it was very important. Before I got to sleep I noticed that the coloured visions returned when I shut my eyes. (Normally I have hypnagogic visions after several minutes in a darkened room when I am tired). I slept well.

Next morning, although I had only slept a few hours, life seemed good. Colours were bright and my appetite keen. I was completely aware of the possibilities arising from the experiment. Colour had extra meaning for me. Voices, typewriting, any sound was very clear. With those whom I felt did not appreciate the importance of the new discovery I could have easily become irritable, but I was able to control myself.

H. O.'s Second Adrenochrome Experience 16. *x*. 53 (*p. m.*).

I had 5 mgm. of adrenochrome this time because we thought that it was probably deteriorating.

I saw only a few visual patterns with my eyes closed. I had the feeling that there was something wonderful waiting to be seen but somehow I couldn't see it. However, in the outside world everything seemed sharper and the Van Gogh was three dimensional. I began to feel that I was losing touch with everything. My sister telephoned and, although I am usually glad to hear her voice, I couldn't feel any warmth or happiness. I watched a group of patients dancing and, although I enjoy watching dancing with the envious interest of one who is clumsy on his feet, I didn't have a flicker of feeling.

As we drove back to Abe's house a pedestrian walked across the road in front of us. I thought we might run him down, and watched with detached curiosity. I had no concern for the victim. We did not knock him down.

I began to wonder whether I was a person any more and to think that I might be a plant or a stone. As my feeling for these inanimate objects increased my feeling for and my interest in humans diminished. I felt indifferent towards humans and had to curb myself from making unpleasant personal remarks about them. I had no inclination to say more or less than I observed. If I was asked if I liked a picture I said what I felt and disregarded the owner's feeling.

I did not wish to talk and found it most comfortable to gaze at the floor or a lamp. Time seemed to be of no importance. I slept well that night and awoke feeling lively, but although I had to attend a meeting that morning, I did not hurry myself. Eventually I had to be more or less dragged out of the house by Abe. I had to get my car from a garage where it was being repaired. There was some trouble about finding it in the garage when at last I was seated in the driver's seat I realized that I couldn't drive it through traffic, although quite able to do so usually. I did not, however, feel anxious or distressed by this but persuaded the garage proprietor to drive me to my destination. I would, I believe, have normally found this a humiliating situation. I did not feel humiliated.

I attended the scientific meeting, and during it I wrote this note : " Dear Abe, this damn stuff is still working. The odd thing is that stress brings it on, after about 15 minutes. I have this ' glass wall other side of the barrier ' feeling. It is fluctuant, almost intangible, but I know it is there. It wasn't there three quarters of an hour ago ; the stress was the minor one of getting the car. I have a feeling that I don't know anyone here ; absurd but unpleasant. Also some slight ideas of reference arising from my sensation of oddness. I have just begun to wonder if my hands are writing this, crazy of course."

I fluctuated for the rest of the day. While being driven home by my psychologist colleague, Mr. B. Stefaniuk, I discovered that I could not relate distance and time. I would see a vehicle far away on the long, straight prairie roads, but would be uncertain whether we might not be about to collide with it. We had coffee at a wayside halt and here I became disturbed by the covert glances of a sinister looking man. I could not be sure whether he was " really " doing this or not. I went out to look at two wrecked cars which had been brought in to a nearby garage. I became deeply preoccupied with them and the fate of their occupants. I could only tear myself away from them with an effort. I seemed in some way to be involved in them.

Later in the day when I reached home the telephone rang. I took no notice of it and allowed it to ring itself out. Normally, no matter how tired I am, I respond to it.

By the morning of 19.x.52 I felt that I was my usual self again.

Subject's Comment.

I shall make no attempt to elaborate or discuss these two experiences. I am satisfied that they represent a model psychosis, but each reader must decide for himself on the evidence of what I have written and what my colleagues report.

Observations by A. H. and N. A. on Subject H. O.'s Reaction to Adrenochrome.

Within 15 to 25 minutes of receiving the adrenochrome injection H. O. was preoccupied with the distasteful colour of the laboratory. He had never before made any comment concerning this. After he had described some of his experiences to us we showed him a reproduction of a Van Gogh painting which he observed very carefully for a long time. It was difficult to divert his attention toward some Rorschach cards we wished him to see. He stated they were not nearly as interesting. But when he did consent to examine these cards he refused to change cards until ordered to do so. Continual persuasion was needed to get a response. For this reason no complete evaluation of the protocol was obtained. However, in response to upper centre D section of card No. 10 he gave the response "these are shrimps, no they are statesmen—they are shrimp statesmen." This tendency toward contamination or the process of loosely combining two associations is not typical of H. O. who normally tends toward high F plus per cent. On the other hand, in word association tests under normal conditions, H. O. does give above average distant responses but is able to report the path of the associative process with no difficulty.

The change in H. O., marked by strong preoccupation with inaminate objects, by a marked refusal to communicate with us, and by strong resistance to our requests, was in striking contrast with H. O.'s normal social behaviour.

On the occasion of H. O.'s second trial the most noticeable objective change was his withdrawal from people. After the laboratory session we drove to the home of A. H. H. O. entered, found a chair where he sat for approximately one hour intently examining the rug. He did not greet the group of people who were at the house nor enter into the discussion.

H. O. was anxious and fearful on retiring and once was found wandering about. In the morning he was easily distracted. He required two hours to dress.

Briefly, the changes noted were preoccupation with inanimate objects, negativism, loosening of the associative process, anxiety and distractibility.

DISCUSSION.

Adrenochrome is the first substance thought to occur in the body which has been shown to be a hallucinogen. Until it was discovered these peculiar properties had only been found in compounds derived from plants, whether from the peyotl (mescalin), or from an African bean (ibogaine), or from a jungle vine (harmine), or from rye rust (lysergic acid), or from the historic Indian hemp (hashish), or from that mysterious fungus *amanita pantherina**, which has tempted so few investigators, and whose active principle is completely unknown. The exotic nature of the hallucinogens catalogued here has made it possible for the sceptic to deny that anything like them could occur in the body, a rash assumption when we know that the body is capable of prodigous feats of chemical synthesis. It is now more difficult to assert that adrenochrome, or something like it, could not accumulate under certain circumstances, and produce devastating psychological disturbances long before any consistent physiological changes could be observed.

It is still a far cry from this to proving that over production of adrenochrome, or something like it, occurs in schizophrenia. However, we have shown that it could be adrenochrome, an immediate derivative of adrenaline.

* Since this paper was written Mr. Aldous Huxley has given us an account of the preparation of *amanita pantherina* which may explain why it has not commended itself to western experimenters. The active principle is excreted in the urine of those who have ingested it. The hospitable Siberian chews the fungus himself and then offers his most favoured guest a brimming bumper of his urine. The hallucinogenic substance remains potent after four to five passages through the human body so that when one has enjoyed it one passes it on to someone else. Amongst the Siberians, less honoured guests receive the hallucinogen after it has been used by several others. It only remains now to carry out this experiment with schizophrenic urine.

At this point somebody usually says " how can you explain such a complicated illness manifesting itself in so many ways, by such a simple mechanism?"

Those who put this question are often surprised to find that we have also thought about this. If one agrees that M substance could exist then there is no reason why it should not produce a wide variety of clinical pictures.

We have listed ten of the variables involved and there are probably more :

(1) The cultural setting.
(2) The personality of the patient.
(3) The age of onset.
(4) The rate of production of M substance.
(5) The quantity of M substance produced.
(6) The exact compound or compounds produced (small changes in chemical structure causes great differences in their physiological and psychological effects ; *e.g.*, adrenaline, noradrenaline, adrenochrome, amphetamine, mescaline).
(7) Specific localization of cerebral enzymes inhibited by M substance.
(8) The capacity of the body for storing M substance. (It is believed that some adrenochrome is stored in the red cells of the blood and other tissue cells (2).)
(9) The capacity of the body for detoxicating or destroying M substance.
(10) The success which the sick person has in dealing with the psychological disturbances produced by M substance. (This very important variable is partly determined by culture. A person, who has a frame of reference which allows him to deal with astonishing experiences, is less likely to disintegrate under the stress of a psychotic disturbance than one who has not.)

It would be possible to elaborate this but at this time it is not relevant.

Only when M substance has been isolated and identified can we begin to understand the mechanisms which produce schizophrenia. Once we understand these mechanisms it may be possible to design a rational treatment based upon exact knowledge, and not, as at present, upon guesswork.

Although we have answered our original question, in doing so we have posed many new questions.

There is the immediate question whether adrenochrome itself plays any part in schizophrenia. This in itself will be hard to answer because we have to search for a fairly unstable compound in a concentration of about one part in five million.

Then where exactly does adrenochrome inhibit cerebral metabolism? What is the meaning of the E.E.G. change which we have observed? What can we learn from the strange psychological changes in mood, perception, thinking and behaviour? And each of these questions, in itself, is the forerunner of a whole series of other questions. At present we cannot answer any of them, but perhaps as Archibald MacLeish pointed out :

" We know all the answers, the answers,
It is the questions we do not know."

The importance of a hypothesis may lie more in the questions which it allows us to ask than in the answers which we receive.

SUMMARY.

Using a hypothesis first published in this journal last year the authors and their colleagues of the Saskatchewan Schizophrenia Research Group have shown that adrenochrome, a derivative of adrenaline, has psychological properties similar to those of mescaline and lysergic acid. This is the first time that a substance which probably occurs in the human body has been found to be active in this way. Adrenochrome has also been shown to produce E.E.G. changes in normal and epileptic people and to inhibit the aerobic and anaerobic respiration of brain tissue in the Warburg apparatus. Future work in this field is discussed. Those who wish to work with adrenochrome are warned of certain dangers.

ACKNOWLEDGEMENTS.

The authors gratefully acknowledge the advice and support received from the members of the research unit and especially A. Szatmari, M.D., for permitting us to record E.E.G. tracings of work which will be published and N. Agnew, M.A. for participating in the psychological trials of adrenochrome and in reporting them here.

APPENDIX.

For those who Intend to Work with Adrenochrome.

If we are to learn more about schizophrenia, experiments with volunteers are essential, but these must be done with proper care. The toxicity of any sample of adrenochrome must, of course, be determined on animals, using the usual methods. Since it is a very unstable substance only freshly prepared solutions should be used. The solution should be mixed with the subject's own blood before intravenous injection; failure to do this results in great pain. We do not at present know why this should be.

It seems to us that adrenochrome's most dangerous properties are psychological ones. Subjects who have been given mescaline or lysergic acid cling to the essential experimental nature of their experiences, and derive considerable help by reassuring themselves that they will soon be over it. Those who have had adrenochrome appear to be liable to lose insight quickly and become unable to relate their experiences to the injection which they have received. It may be that the insidious nature of adrenochrome's action erodes insight, or perhaps it has some specific property which the others do not possess. Whatever the cause this loss of insight requires special care. Until we know more of this new model psychosis (to use Fischer's excellent term) produced by adrenochrome, it would be prudent to assume that it will be effective for at least 24 hours and to supervise the subject for that period of time. It is possible, though not certain, that large doses of niacin (1 gr. by mouth or 100 mgm. intravenously) may counteract the effect of adrenochrome.

In selecting volunteers we suggest that, until more is known about adrenochrome, those with a bad family backround, who have history of liver disease or psychotic episodes, or whose Rorschach responses are suspicious should for the moment be excluded. Close supervision for 24 hours should include an absolute refusal to allow the subject to drive a car. We have some evidence that the capacity to relate time and distance may be subtly disturbed by adrenochrome. This could be disastrous.

We do not wish to appear alarmist, but believe that we should make other workers in this field aware of some of the troubles that we have encountered. It seems to us that we have a special responsibility to those who are prepared to trust us with the temporary custody of their minds and bodies to further man's knowledge of himself.

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ANTERIOR CINGULECTOMY IN SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS: CLINICAL RESULTS.

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Recent interest in the surgical alleviation of mental disorders has centred in the trial of new and different operations. Fairly early in the development of the subject Freeman and Watts (1944) themselves reported the fairly constant observation that under local anaesthesia gross mental change did not occur until certain stab incisions had been made deep in the infero-medial quadrants. Marked mental change, with confusion, unresponsiveness and disorientation, seemed to occur on section of a small bundle of fibres located inferiorly close to the midline. Most of the modifications of Moniz's original procedure have, however, been made on an essentially empirical basis.

Anterior cingulectomy as an alternative to frontal leucotomy was suggested by the behaviour changes recently observed in monkeys. Experimental ablations in this region led to marked alterations in "emotional" behaviour (Smith, 1944, 1945; Ward, 1948; Glees *et al.*, 1950). What little clinical evidence there is for the functions of this area in man also suggests that it may possibly mediate some of the beneficial changes observed after full frontal leucotomy.

On the other hand, the important evidence of Meyer and McLardy (1949) from careful correlation of anatomical and clinical data, suggests that bilateral involvement of area 24 or of the agranular part of the posterior orbital region does not contribute to improvement; on the contrary, it seems if anything to militate against it. But so long as we continue to operate for these disorders we must try to find specific operations.

Accordingly, in 1948, the late Sir Hugh Cairns started performing the operation of anterior cingulectomy, and all the early work was done under his personal guidance. The lesion in the cingulate gyrus is made by suction ablation; the first subjects were severely psychotic patients in whom all other treatments had failed. Details of the operation, with early results, have been briefly reported elsewhere (Whitty *et al.*, 1952).

This report is essentially a description of the effect of anterior cingulectomy on schizophrenic illness: for among the few cases not actually diagnosed as schizophrenia there were still many features of a schizophrenic nature; and the number of examples of other illnesses are too small to yield reliable information.

We have diagnosed ten cases as schizophrenic, one paraphrenic, one an aggressive oligophrenic, and one a presenile dement. The only cases of affective illness were two agitated melancholics. There was also one post-encephalitic psychopath and one psychotic epileptic. This makes seventeen patients aged between 18 and 68, with an average age of 38. Thirteen (approximately 75 per cent.) had been ill for over five years ; nine (approximately 50 per cent.) for over ten years. The extent of the ablation from case to case necessarily varies slightly, though in all cases it extends backwards from an anterior limit level with the tip of the corpus callosum (Fig. 1), and every attempt was made to make the lesion exact. The lengths of the lesions were measured at operation : five were 1 cm., four were 2 cm., 25 were 3 cm. This makes up the 34 separate ablations on the 17 patients. The histories follow.

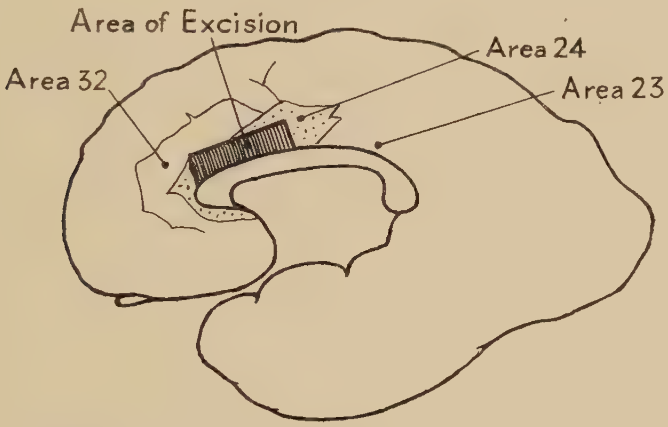

FIG. 1.—Diagram of medial surface of brain and area of operative removal.

CASE 1.—*Male, aged* 34 ; *a Post-encephalitic with Aggressive and Criminal Tendencies.*

After his mother's death, when he was a baby, he was looked after by various foster-mothers, and then a step-mother who probably ill-treated him. He is said to have been a very difficult child. At 8 he had encephalitis lethargica. It is not clear to what extent his behaviour was difficult before the encephalitis. At 11 he was committed to an approved school for stealing, and never made a subsequent satisfactory social adjustment. He either failed, as in the Army and the Merchant Navy, on medical grounds, or, more frequently, through frankly anti-social behaviour. In personal relationships he could be pleasant and attractive. Five years before operation he had married the daughter of a clergyman. She was pregnant by him at the time. That the marriage had a rather stormy course is hardly surprising, but reconciliation followed each breakdown. His wife was very fond of him and persuaded him against leucotomy when first suggested. He was suspected of one or two sexual aberrations, including homosexual behaviour.

He entered hospital as a voluntary patient, after a suicidal attempt five years before operation. He exhibited a syndrome of post-encephalitic Parkinsonism with fixity of expression, blinking and wasting of the left leg. Mentally he was depressed and unhopeful, worried about his unhappy marriage and financial stress he confessed to suicidal leanings. With continuous narcosis he improved and even became euphoric, but a paranoid attitude emerged for the first time. He felt people were against him, and discharged himself seven weeks later.

He continued to be extremely depressed, pessimistic, hostile and paranoid in attitude. He decided to strangle his wife. The attempt was unsuccessful and he was again admitted. After further violent and paranoid behaviour a leucotomy was performed three years after his first admission. His main diversion now became stealing bicycles and cars, interspersed with impulsive aggressive outbursts, and there was a general worsening of all his behaviour. He went once to prison and twice to a mental hospital as a voluntary patient. Finally he was certified and admitted again. He was hallucinated and deluded. He said there were voices saying " nasty things " about him. He was extremely irritable, impulsive, paranoid, resistive, and his dirty habits included throwing faeces. He continued to deteriorate, had marked delusions of persecution, smashed windows, and threatened persons, or attacked violently. He had to be transferred to a padded room. Three years after leucotomy he had one *grand mal*. His extremely hostile behaviour with frequent violent outbursts and attempts to escape continued up to the time of cingulectomy.

After operation the patient was well behaved, but demanding of attention. He appeared cheerful and there was no obvious intellectual impairment. He became restless, but general improvement continued. He attended church, films and dances in the hospital; worked on the ward; was happy and sociable and given progressively more liberty. Soon he was working out in the gardens, and although the ultimate prognosis could not be deemed really hopeful it was eventually decided to try him with a job outside hospital. A week later he absconded in a doctor's car and was found in his brother's house. After this he became depressed, uncommunicative and remorseful This was in contrast to his relative lack of affective response up to this time, but he continued for some months to be quiet and well behaved. He was sociable with other patients and showed considerable aptitude at occupational therapy.

Fifteen months after the operation he left hospital. He stole a car and was sentenced to three years' corrective training, but because he repeatedly abused privileges he was sent to an ordinary prison. He again became sullen, demanding, and his insight was now poor. Though he was never now impulsively aggressive towards persons, he had lost all his cheerful sociability and his behaviour is unpredictable as before.

CASE 2.—*Male, aged* 24; *a Catatonic Schizophrenic.*

From childhood this patient was something of an unhappy misfit, the butt of his bad-tempered father, and the odd one out among his school fellows. At his convent school he was sensitive and solitary, yet bad-tempered and often resentful of punishment. He was mentally backward, nervous and apprehensive, and developed as a nervous, nail-biting child, who cried at night and sweated so much that the bed was invariably damp. He could not read when he left this school at 11, and was backward at spelling and arithmetic, though he could write. Soon his family noticed his pronounced avoidance of people. He would walk to work so as not to meet them on the bus and would go out for walks at nights only. He said his work-mates were discussing him. He would spend a good deal of his time staring. At other times he would seem very anxious and tense.

Away from home he began to drink and mismanage his money so that his mother had to visit him to straighten out his affairs. He changed jobs about every six months and his work record was generally bad. He became increasingly self-absorbed with behaviour which was fatuous and slightly bizarre. He became excessively interested in religion. At 18 he made a threat of suicide and was admitted to hospital, hallucinated and complaining of occipital pain and fears of " having tuberculous space." His behaviour varied from fatuousness and grimacing to apprehension, but he was always withdrawn.

His condition was not changed by a course of ten E.C.T.'s After five months he left, but was returned the following month under certification. He imagined that people would kill him, and he had episodes in which he was severely hallucinated, tense, and anxious and repeatedly complained in a frightened way that there was something wrong with his head and heart. Under narco-analysis he gave a typically schizophrenic account of his feelings. He had one epileptiform seizure. He was given continuous narcosis both with paraldehyde and sodium amytal and further E.C.T. but continued to deteriorate. His behaviour fluctuated between fatuousness and tense apprehension, and hence with disturbing delusions and impulsiveness.

Immediately after operation he showed a marked decrease in anxiety but increased apathy. He was, however, pleased that his mother was visiting him. He showed temporary incontinence of urine, rather animal-like eating, and repetitive purposeless movements. He denied delusions. He answered questions, but replies were retarded if they required thought.

He was alternatively apprehensive and apathetic, sometimes insolent, but gradually he improved, especially in behaviour, and by the end of the second month he was transferred to a better ward and was attending occupational therapy regularly. He needed no drugs, in contrast to his previous heavy doses. For two months his rapport and behaviour were better than they had ever been in hospital, but then he again showed occasional aggressiveness and became more impulsive. He jumped out of a first storey window, and he smashed a picture " because it got on his nerves." He appeared anxious and preoccupied, and for a while was stuporose, adopting fixed postures for hours, and dribbling saliva. He was unresponsive to questioning, resistive, and he often refused his meals.

Although he recovered from this he remained withdrawn and indifferent. After a week of mild euphoria he was by six months after operation again inaccessible and inactive, and indifferent to the visits of his relatives. He was noticed to be more full of life after an epileptic fit which occurred nine months after operation. This was followed by three other fits with vomiting half an hour after. He was put on anticonvulsant drugs, but from then on had a fit about every two months. The only residual improvement was that he no longer complained of his hypochondriacal fears and the nursing staff found him quieter and less tense. He shows spasmodic but shallow interest in outside activities.

CASE 3.—*Female, aged* 53 ; *an Imbecile, with Aggressive Behaviour.*

Although mentally defective from birth she had worked successfully as a domestic until a suicidal attempt at the age of 42, which brought her into hospital. She was then depressed and retarded, and was noticed to be markedly childish, slow and "weakminded." She was silly and irresponsible and unfit to look after herself. She had probably had one or two fits in early adolescence.

Altogether she had been admitted six times to a mental hospital, but between her bouts of uncontrollable behaviour she worked as a cook-general. She had fluctuated between aggressive mania and moderate depression, with occasional attacks of more severe depression and suicidal leanings. Gradually noisy and abusive outbursts were more frequent and she began to strike patients. Once she attempted to strangle a nurse, and later succeeded in throttling another patient. She became very resentful of any discipline, whether real or imaginary, though still had quiet periods when she would work well. She had heavy barbiturate sedation and a course of narcosis but it hardly affected her. She continued to display violent aggression, which was the main indication for trying cingulectomy.

She was quieter and less talkative immediately after operation. She answered questions much more freely and obeyed orders, but made no attempt whatever to occupy herself. She had 12 *grand mal* attacks after operation and was put on phenobarbitone gr. 1, *b.d.* and epanutin, 0·1 gr. *t.d.s.* The fits ceased. She gained 7 lb. in weight. She said, " I can control myself better ; if annoyed I move away." She slept better with much less barbitone. For four months she was well-behaved, cheerful and co-operative. She was pleased when her sister came to visit her, and disappointed at not being sent to a better ward. Three months after operation she was transferred to the best female ward, and immediately responded well, becoming more pleasant and sociable, sitting chatting with other patients. She remarked that she never now had feelings of anger which she used to have. She attended hospital functions, enjoyed them, and wanted to go home, though she showed no disappointment at not having gone already. All agreed that she was now decidedly better.

Six months after operation she relapsed badly, suddenly provoking other patients and attacking both patients and staff. She refused absolutely to work. She once attacked her sister on a visiting day. Put on sodium barbitone she became drowsy, but still aggressive and rude when disturbed. She had to eat alone, and would sometimes smash crockery and throw it about. On the whole she became even more unpredictable; would not work; and was on as much as 30 grains of barbitone a day. On the whole her behaviour in the attacks was less violent and intense than before operation, but was so unpredictable and so little improved in general that a year later she had a standard leucotomy.

CASE 4.—*Male, aged 28; a Catatonic Schizophrenic.*

The third of eight children with a normal family background, as a child he was timid, credulous, shy and easily led. He was dull at school but good at games. Once he attended a child guidance clinic. At his first job as a house-boy in the house on a big estate he felt keenly his first separation from home, which showed itself in his fears of the dark and sleeping on the ground floor. He became very timid and frightened. In his second job as a hall-boy in a private house, he soon said he felt unequal to it and a few days later was sent home in a stuporose state. At home he talked strangely, had outbursts of unreasonable anger against his mother and sister, refused food, became increasingly hostile and noisy, and was admitted, certified, at the age of 16.

He was mute and resistive, and seemed very frightened. Leptazol treatment was begun and after the first ten he improved. He had 17 more convulsions but from then on remained relatively static.

When discharged three months later he was alert and cheerful and able to work around the house. His talk was rational but lacked spontaneity, and from this time he was recognized as abnormal in his behaviour and social adjustment. Though he held some jobs he was simple, childish, and easily led, once being induced to steal an ambulance. He was rejected for military service and began to brood on this, becoming even more withdrawn and irritable. He made two attempts to hang himself, one at home and one at work, giving as his reason " that he had said Jesus to himself."

He was readmitted, withdrawn, limited in ideation and retarded in thought. After several attempts to escape, he was transferred to a locked ward. With electro-convulsant therapy improvement was very slight. He escaped, broke into a house in the hospital grounds, and committed several acts of useless destruction. He was hallucinated but would rarely admit it. Periodic electro-convulsant therapy made him less destructive but effected no real change, and up to the time of operation his conversation was mechanical and stereotyped, he perseverated markedly, and was largely out of contact with reality. He had altogether 60 electrically induced convulsions apart from those induced by leptazol. He was restless and anxious, with aggressive outbursts.

For three months after operation he was much less withdrawn and more rational, though still restless. He perseverated less. He no longer needed sedative drugs. His answers to questions were more forthcoming and more relevant. He was not destructive or aggressive and came out of strong clothing for the first time for years. He was occasionally incontinent but generally behaved well and went to pictures, dances and social functions. He had stopped masturbating.

Six months after operation he was still a little more forthcoming in conversation, and less destructive, but he was obviously steadily relapsing. He became inaccessible, but still worked and behaved co-operatively. Within a few more weeks, however, he was again aggressive and subject to violence. In outbursts his violence was less intense. The only other change was that he was possibly less slovenly and dirty. In this state he has remained.

CASE 5.—*Female, aged 54; Paraphrenic.*

A married woman, of 54, previously normal, who for 12 years before admission had been having bouts of mental disturbance about twice a year lasting some two months, during which she was excited, refused to leave the house and talked incessantly to herself, usually about the past. Sometimes she would become unpleasant and quarrelsome with friends and neighbours, and swore. She had even turned against her husband and daughter, making accusations against them and attacking them. She accused her husband of going out with other women and of his being the father of her daughter's child. She has sometimes locked the daughter out of the house. In between these bouts she would appear to be quite normal. In 1944 she had a partial thyroidectomy.

She was eventually admitted under certificate three years before operation, in a deluded and hallucinated state. In hospital she was un-cooperative, hostile and aggressive towards others and suspicious of their movements. She attacked other patients, but often was well behaved for weeks at a time. A course of E.C.T. produced only the slightest improvement. During one of her better periods she was out on trial but had to be readmitted. Over the next two years she had ups and downs and was in and out of hospital several times. She was a pyknic in build and there was a marked cyclical character in her illness. Excitement was a prominent feature and her delusions and hallucinations showed no systematization. However, the paranoid trends were becoming more fixed and her behaviour increasingly aggressive. Her personality was fairly well preserved and a decision to leucotomize her was changed in favour of cingulectomy.

For three months after operation she was still having periodic outbursts of abusive and aggressive behaviour. She imagined insults and sneers and on one occasion attacked a doctor. The nurses considered her easier to manage in between outbursts, and for a time she had week-end leave and seemed quite well.

She soon relapsed and had to return. The pre-operative pattern of her illness has not changed. She is alternately quiet and industrious and noisy, suspicious and aggressive. The nursing staff find her more manageable in her outbursts and she works more effectively in between. She has in no way deteriorated and there have been no post-operative complications.

Case 6.—*Male, aged* 41.

At the age of 11 he went to a Roman Catholic special school for mental defectives and remained there until aged 15, when he was removed by his father to avoid certification as a mental defective. He was home for four years but failed to keep a job; he was discharged from the Army as mentally deficient. At 19 he returned certified to the Institution and later came home on licence to his parents. He took a job washing City buses which he held for two years and saved £100. At the age of 30 he was discharged from certificate, but after this he became increasingly solitary, aloof and resentful. He had frequent noisy violent quarrels with his father, which neighbours reported to the police, and which led to his admission to Littlemore when he was 32.

In hospital he was quiet at first and worked in the garden, but a year after admission he became sullen and hostile. He displayed delusions about his father and the Germans and from this time on he remained resistive, threatening, and inclined to incite other patients. His abusiveness made it necessary to send him to the refractory ward. Mental testing showed him to be of low intelligence. His general knowledge was fairly good and his interests unusual for a feeble-minded man. He read papers and novels, helped to do plays, and a certain amount of translation from French, anglicizing French words he did not know. He read poetry very well, with correct rhythm and intonation. He would say, " Which would you prefer, doctor, Hitler's love or England's slavery ? This country keeps me in serfdom ; it ties me down to postage stamps and other people's labour."

After eight years in hospital his paranoid ideas were becoming more rigid, his sense of grievance was strong and there was a good deal of bitterness underneath his aggressive attitude, making him tense and unhappy. The increasing hostility and violence of his behaviour threatened to preclude him from the dramatic and other activities in which he seemed to take some pleasure. He was not excessively deteriorated and cingulectomy was preferred as surgical treatment.

For a while after operation he was quieter and less belligerent ; in conversation his paranoid ideas were still present, but had rather to be dragged out. He behaved well with sedatives and did a little ward work, played cricket and for a month seemed to have less tension and unhappiness from his ideas.

However, this improvement did not last and three months after operation he had to be put on amytal for his anxiety. He was again hostile, bitter and paranoid, and his ideas were stereotyped and habitual, with a good deal of tension. He was regarded as quieter in behaviour, and could now more easily be humoured. Six months after operation he was obviously in a state of considerable distress, and a standard leucotomy was performed.

CASE 7.—*Male, aged* 31 ; *Hebephrenic Schizophrenic.*

This was a single man who had shown very early signs of mental illness and at his first job on a filling station was noticed to be laughing and giggling. Three months later, at his second job, he was sent home because of perpetual behaviour of this sort. He sustained a severe burn from an accident soon after this and was from then on rather more withdrawn, foolish and manneristic. He gradually became more bizarre in behaviour and was eventually mute and destructive. He was admitted as a voluntary patient at the age of 17 and soon became quieter and left hospital. Only a few months later he was readmitted following a suicidal attempt. On this occasion he had no activities whatever, did not read, write or talk ; he would lie in bed with the clothes pulled over his head and not reply to questions. On occasion, if he were aroused, he would look greatly alarmed and even terrified, become obscene and hurl abuse. There was marked disorder of though, and some apparently disturbing delusions.

He became increasingly destructive, aggressive and abusive, and was quite withdrawn from reality. His apprehensive attitude continued. On account of this, combined with his increasing violence and general deterioration, he was recommended for operation. He had failed to respond to five courses of chemically and electrically-produced convulsions.

After operation he was for a while quieter and even responsive. He showed a considerable interest in what was going on around him, talked to people, and read magazines and books which were brought to him. He also lost his apprehensive, frightened look. After a while, however, it became apparent that operation had not altered his basic clinical picture. He was incontinent of urine for some while. He soon had to be returned to the same refractory ward and was again hurling abuse and adopting a very aggressive attitude. It was, however, noticed from the beginning that in the aggressive outbursts he was much less violent and, though he did make attempts to smash things, he now no longer tried to run away. After three months he again became slovenly, mute, manneristic and quite withdrawn, and had relapsed almost to his pre-operative condition ; his less purposeful and less directed behaviour in his violent outbursts made him generally more manageable and predictable.

CASE 8.—*Female, aged* 44 ; *a Hebephrenic Schizophrenic.*

This was a Jewish refugee who came to England in 1938 after persecution in Germany. She was admitted for the first time ten years ago after violent outbursts of temper. She was depressed, restless, irritable and resented questions, but there was no thought disorder. She had E.C.T.'s without improvement. She became more aggressive and assaulted the staff, though her underlying personality was perfectly well-preserved and she conversed quite rationally.

She had much physical treatment but continued to deteriorate. She was hostile, would attack other patients and staff, and walk round the back court shouting and pouring forth a string of obscene statements. She was feeding herself, but was incontinent at times both of urine and faeces. In between her hostility and violence with hallucinations she would have periods of pleasant, sensible conversation. She was never suicidal. She seemed to know the value of good conduct in obtaining privileges, but was never spontaneously friendly. Though her basic personality was quite well-preserved, she was becoming more and more distracted by her "voices." Except for occasional lucid spells, usually when a doctor was present, her contacts with reality were limited to hurling abuse and obscenities on all who came near her and making vicious, unprovoked attacks on them.

After operation she remained noisy and abusive and was still preoccupied with hallucinations. She remained resistive and noisy, and if anything she was even more wild in her movements and more difficult to engage in conversation. In contrast to this, in a small group out in the village it was noticed that she was much quieter and more controllable when shopping and now did not try to run away or attack the others. This applied also when she was dancing or at the cinema or when allowed some special privilege. She worked quietly.

A year after operation she was easier to manage, still hallucinated, noisy and aggressive, but she made no specific attacks on other patients, and from now on became gradually better. Her noisy outbursts were reported as less frequent than before operation ; there was no incontinence or fits. She was not on medicine and she slept peacefully. She would help with the laundry in the ward and would talk with the staff, though she would still not talk with other patients. She had slightly better contact with her surroundings, took some interest in newspapers and magazines, and showed some interest in her clothes. She talked more rationally when approached, but was never spontaneously sociable. She still says the "voices" annoy her, and will still shout obscenities on occasions.

CASE 9.—*Female, aged* 20; *an Aggressive Epileptic of Low Intelligence.*

Coming from a squalid and dirty home, with two sisters of low intelligence, this girl was well-behaved at home as a child, but a teacher considered her behaviour difficult and aggressive at school. As she grew up she became increasingly difficult and aggressive: she attacked a sister's child, with the intention of killing it, and was removed to an institution from which she came to the mental hospital two years before operation. She would shout and sing, and had frequent noisy outbursts in which she attacked the nurses by clawing, biting, kicking or any violent means at her disposal. In between attacks she was clean, childish, and inclined to giggle. Usually she would do no work. In any case she could only do the simplest tasks and answer the simplest questions. There was no evidence of delusions or hallucinations.

Before operation she was having about 14 major fits a month, almost always at night, and about the same number of minor attacks. Her aggressive outbursts seemed to be unconnected: they occurred four to five times and might persist for hours unless terminated by apomorphine. Usually she sang loudly and attacked the nearest person to her. She needed heavy sedation: if drugs were stopped fits and outbursts were more frequent.

After operation she improved. When her first outburst occurred three weeks after operation it was at once apparent that she was much less violent and seemed to have much more insight into her abnormal behaviour. She was quieter and took more interest in people and things about her. She would converse more spontaneously within her rather limited range of ideas. She noticed changes in her environment.

By two months post-operatively she was considered more alert, was cleaning windows and performing other useful tasks with efficiency. She was sociable: she went to dances and the cinema and seemed to enjoy them.

Between three and four months after operation she returned to her preoperative state. She had violent outbursts: once more she attacked nurses and patients. After the first phase of her outbursts she was little more easily pacified than before. She seemed to be as sly, cunning and jealous as always, and still had to spend a good deal of her time in the side room. She was never incontinent. She had one *grand mal* attack a month after operation and was put on epanutin. A week later she had 6 *grand mals* and was started on phenobarb., gr. 1 *t.d.s.*, and after this remained free of fits for three months.

For the next two years she had major attacks regularly, but at an average of six a month compared with 14 before operation. Since then she has been having them even more frequently, with an average of over 20 a month.

CASE 10.—*Female, aged* 18; *Catatonic Schizophrenia.*

She was one of 10 children and came from a poor family. She was a very good child, but shy and solitary and backward at school. However, she learned to read and write and held two jobs, as errand girl and shop assistant, after she left school. In her work she was slow and untidy but showed no eccentric behaviour. At home, however, she was morose, irritable and could not sleep. Two years later she became noisy, incoherent and had aggressive, violent outbursts alternating with stupor. She was admitted certified at the age of 16 in a state of acute catatonic excitement. She ignored all questions, resisted nursing attention and made such violent attacks on the staff that she had to be secluded in a side room. No delusions or hallucinations were elicited. A course of six electrically induced convulsions was followed by 30 insulin comas, with slight improvement, and she was able to attend occupational therapy; but she remained fatuous, defective in habits and liable to violence, and three months later she relapsed into a full state of catatonic excitement, which lasted up to the time of operation 18 months later.

She was violent, restless, abusive, shouting obscenities, smashing windows, and running about the courts tearing her clothes or taking them off; three or four times a day she would make sudden vicious attacks on patients and staff, which seemed to give her pleasure. These attacks did not seem to be a response to hallucinations or delusions. Generally mute and inaccessible, she would sometimes obey simple commands or give monosyllabic answers, but she would not talk to other patients or visitors. She would adopt distorted postures but never maintain them for more than a few minutes. She was incontinent, had to be kept in strong clothing in a locked ward, and had to be heavily sedated day and night with veronal. This was her state at the time of operation.

For two months after operation her violence subsided into passive resistance, she would not go where the nurses told her and would lie down on the floor and refuse to get up, but she did not attack and ceased to break windows and tear her clothes. She knitted, and asked for a lipstick and a pretty dress and formed an attachment to a nurse though she still ignored other patients. She ate ravenously and grabbed at her food, but used a knife and fork. Incontinence decreased and drugs were reduced. She had no major fits, but occasional *petit mals* were suspected. After two months she became increasingly resistive. She would no longer knit and became slovenly in her appearance and was incontinent. She was withdrawn and fatuous, and walked about restlessly. Six months post-operatively her brief improvement had receded except that she was less violent and she was apathetic rather than restless. A year later she was again violent and deteriorating.

CASE 11.—*Female; Paranoid Schizophrenic.*

She was an illegitimate child, whose mother had married when she was four. Until she was 12 she believed her step-father was her father and became hostile when she learned the truth. She was a prim, fastidious child, who held aloof from other children. She was jealous of her siblings, self-centred and very ready to stand up for her rights. She had typical adolescent interests but did not mix easily and had "crushes" on older men only.

At 21 she became pregnant by her fiancé, a young man whom she did not love. Despite her mother's assurance of support, she insisted on marrying him. She kept her house beautifully and was a good mother to the child, but she and her husband never agreed.

Immediately after a difficult birth of her second child, her mother noticed an unnatural "demented" expression. She complained of "bad nerves" and behaved unpredictably. She was aggressive even to her mother, to whom she had always been devoted, and picked quarrels with her husband, refusing to pack when they had to move house. She developed delusions and became so wild and disorderly that she had to be admitted to hospital. This was three years before operation. She was at this time intellectually clear, but there was poverty of affect. She had distinct delusions of persecution involving her husband, who was said by others to have ill-treated her in their early married life.

She improved in hospital and was discharged. She would not return to her husband and went to live with her mother. She would sit preoccupied for hours and then suddenly do something on impulse. She was restless and quarrelsome. If she met her mother in the street she would ignore her. She could not settle, and moved about during the next 18 months, sometimes working and sometimes living with relatives. She was twice admitted to mental hospitals in other parts of the country.

After being discharged from the second mental hospital to her mother's care she accused her mother of keeping a brothel and claimed she herself was pregnant from intercourse with an unknown man in the night. She accused her step-father of sexual advances. She lost weight rapidly and when admitted again, eight months before operation, she insisted she was pregnant though she was menstruating at the time. Her thought stream was interrupted and there were irrelevant associations with bizarre ideas, She thought people in the street saw that she had had intercourse while drugged, from the lines under her eyes. Her affect was flat and her manner foolish. She was given about 40 insulin comas, but remained aggressive, resistive and suspicious. Her delusions had now spread to the staff, whom she accused of trying to poison her and examine her against her will. She developed distressing hypochondriacal ideas about her genitals, and became anxious, depressed and resentful. Her delusions, though florid and insistent, were but loosely systematized. She had lucid, rational intervals in which she talked and behaved rationally and her basic personality was well preserved.

She was rational and alert after operation, but was annoyed that it had been performed on her head and not on her abdomen. She had seven fits in the first 48 hours, but was not incontinent.

She was more tranquil, but the delusions were still there. She was convinced that something was wrong with her womb, and complained that the doctors did nothing for her. She told the staff that she was pregnant, but ceased to mention this again to her mother. Her affect was now labile. She would by turn be apathetic and indifferent, grumbling and querulous or overtly aggressive. However, she agreed to wear hospital clothes, which she always refused to do before, and helped in the ward.

Hostility to her husband seemed untouched, but she became calmer towards her mother, and asked for the first time about a step-sister, of whom she had always been very jealous. She also enquired about her children. She believed she was retaining food and drink and therefore would not eat. She began to lose weight, and as her delusions were obviously still distressing her she was leucotomized three months after cingulectomy.

CASE 12.—*Male, aged* 30 ; *a Catatonic Schizophrenic.*

This was an intelligent and well educated young man who developed typical schizophrenic behaviour and ideation some three years before admission. He rapidly progressed to a grossly deluded, paranoid, and aggressive clinical state. He developed particularly bizarre religious delusions, and his behaviour fluctuated between a withdrawn, inert state and, more frequently, one of extreme tension and unpredictable impulsive violence. Typically he would smash windows and attack people. He failed completely to respond to other treatments. Occasionally he would for a short time be rational and even pleasant in manner. At the other extreme he would be stuporose, mute, and refusing to eat or drink.

Immediately after operation he was brighter, and even euphoric and grandiose for a time, with a vague optimism about the future. He was properly orientated. He had no incontinence or fits. He ate well, and behaved rationally and socially in a good ward. He sustained an intelligent conversation. Five weeks after operation he smashed three windows and was sent to a refractory ward. He was contrite about this. For a while he was quieter and would work at polishing. However, his schizophrenic thought and impulsive outbursts remained, and he soon refused to eat again.

He became tense, restless and again preoccupied with bizarre religious ideas. His delusions were less systematized than pre-operation. For three more months he remained brighter, and then he became mute, though still liable to aggressive outbursts. He had to be tube-fed, and in general his personality and behaviour were deteriorating rapidly and he relapsed completely to his pre-operative state.

CASE 13.—*Female, aged* 23 ; *Hebephrenic Schizophrenic.*

This was a pretty girl, always very shy, quiet, and mildly studious, who had her first nervous breakdown at the age of 20 following the unwelcome attentions of her employer, a married man. After this she became restless, moody, querulous, sometimes quite silent ; she lost interest in everything except books on psychology, and began doing odd unpredictable things. She would wander in the streets at night alone ; she would walk out of the cinema and leave her friends ; she gave up a boyfriend on some unreal slight pretext.

Her illness developed rapidly and soon she was deluded, excitable, unruly, and eventually attacked her parents, She had to be certified and on admission, aged 21, she was peculiar in manner and uncommunicative except on the subject of the witches and spirits which she said had been troubling her for more than a year, and these witches gave her " urges." Sometimes they appeared in her room as lights. Her affect was incongruous with these ideas.

On insulin treatment she made no improvement, in fact she became rude, aggressive and noisy after this treatment and used obscene language and was commonly truculent and difficult to manage. She was destructive to articles in the ward and would bully other patients.

Her illness generally worsened, though in the 12 months preceding operation her delusions were less evident; but she was profoundly apathetic. She grinned, grimaced, gesticulated, either would not speak or replied to questions in a stilted, expressionless way and with an air of haughty detachment. She was aggressive; in one attack she knocked over an old lady who broke her wrist. Between outbursts emotional flattening was profound; she was not particularly tense. She neglected her appearance, losing her good looks, and appeared to be rapidly deteriorating.

After operation, for about two months, she talked more sensibly and behaved more quietly, though was still aggressive in attitude. But after another month the violent outbursts themselves recurred; she would strike other patients and staff and generally became restless. She was incontinent on several occasions. Six months after operation the attacks were continuing; she was emotionally quite flat in between, and a pre-frontal leucotomy was performed.

CASE 14.—*Female, aged* 42; *Hebephrenic Schizophrenic.*

A dreamy, sensitive girl, clever at her books, she had normal out-going interests but could not make friends and had an unpredictable temper. She was a fervent Catholic and had been upset and bitterly resentful when her mother opposed her resolution to enter a convent. She took honours in her Senior Oxford, but exams were a nightmare to her. She went up to Oxford but was constantly harassed, apparently needlessly, by fears and doubts about her capacity to cope with her work. She was attending Mass daily. At the age of 20 she became acutely ill, with confusion, restlessness and incoherent speech. She became manneristic and impulsive and once rushed naked into the street. She was certified when she was 21.

After 20 years in hospital she had sunk into a vegetable-like existence in a chronic ward, sleeping in a side room and doing no work. She was usually withdrawn, but was subject to aggressive phases, once a month and lasting several days, when she would smash windows and make vicious and cunning attacks on patients and staff. The only emotional reaction she showed was anxiety over unusual situations. She was a constant nursing problem. She was restless at nights, only sleeping very little and doubly incontinent. By day, she was always untidy, had to be hand-fed and needed constant supervision to make her use the toilet. She was quite inaccessible and incapable of carrying on even a simple conversation. She would repeat questions and mimic the gestures of the questioner. She displayed stereotyped mannerisms and postures, genuflected frequently and seemed to be going through various religious rituals. No fixed or distinct delusions could be elicited. Operation was performed as a last resource.

For the first four months after operation she was quieter in behaviour and more in touch with her surroundings. She read the headlines of the newspapers and did a little knitting. Her appetite improved and she was able to sit at table. She was cleaner in habits. She slept better. She was allowed to go to church for the first time in 10 years, and attended hospital functions.

After this initial improvement, she deteriorated, becoming withdrawn, resistive, and again subject to attacks of violence. She was not incontinent, but needed constant supervision. Her appetite remained good and she no longer needed to be fed and she was able to take more part in hospital activities, attending church and dances.

CASE 15.—*Female, aged* 62; *a Presenile Dement.*

An untrained nurse who had devoted her life to caring for an invalid husband who died before her illness began. She became acutely confused and restless while in a general hospital and was admitted under certificate. She was then quite inattentive, rambling in conversation, completely disorientated for time and place, with recent amnesia. This was 18 months before operation, and her condition became worse. She had phases in which she was very agitated and restless and phases in which she was quieter and more composed. Throughout she was confused and disorientated, rather facile in mood, and troublesome in behaviour. She began rubbing food in her hair and for some months was constantly picking at sores on her face and neck. With heavy doses of sodium amytal, up to 15 gr. a day, she picked herself less, but was much more confused. A fairly heavy dosage had, however, to be maintained, or she would become extremely agitated and quarrelsome and attacked anyone who went to help her.

Physically she was thin, but in this period was not losing weight. She was arteriosclerotic, with a pressure of 180/110. She had pigmentation of the face and neck. Often she was doubly incontinent at night. Eventually she required constant nursing supervision. Besides picking her face continually and apparently compulsively, she had other acts which gave the strong outward impression of obsessional ritual. She tapped her head and knee so many times with a toothbrush, and repeatedly put her head down the lavatory. There was no evidence of any feeling of compulsion.

For a month after operation she was in greater contact with her environment and she talked rationally ; though she still rambled on and it was, now, difficult to stop her. She was obviously no clearer intellectually, but could now parry questions aimed at testing her memory. For this month also she had no fits and was never incontinent.

Following this remission she deteriorated rapidly to her old state. Now she was rather more euphoric and facile, but she talked incoherently, was irritable, resistive and hostile ; and her behaviour became dominated by her absurd activities of tapping, picking, and hoarding. She tore her clothes, but she did not now attack people. She was again incontinent, and though she attended occupational therapy and entertainments she was capable of only the simplest activity under supervision.

CASE 16.—*Male, aged 68 ; a Chronic Agitated Melancholic.*

He came of hard-working farm-labouring people. His mother died in a mental hospital after he became ill. One sister had a chronic nervous illness. He had served 12 years, mostly abroad, in the regular army, and was working for a former C.O. when he was called up in the 1914–18 war. He was badly wounded by shrapnel and was invalided out of the Army with a pension of 4*s*. per week. From then he worried continuously about being a financial burden to his parents. He did various labouring jobs and, while building, fell from a ladder. He was not seriously injured but as a result of the " shock " was not able to resume work.

He became markedly depressed, developed hypochondriacal ideas and various delusions about being poisoned. He was so restless and distressed that he could not be looked after at home, and was eventually admitted to a mental hospital at the age of 48, where he remained. Though at first a little better in hospital he soon developed into a chronic, unremitting, agitated, depression. He was tormented by hypochondriacal and other frightening, depressive delusions. He thought he had venereal disease, and that because of him the world was soon coming to an end. He made no social contacts and had no interest in his surroundings. At his worst, usually for about a month at a time several times a year, he was extremely agitated, would not talk, and appeared terrified. Between these times he would talk briefly and rationally, his delusions apparently quiescent. He had had electro-convulsant therapy on three occasions, without improvement.

A year before operation he deteriorated rapidly. He retired completely into himself, did no work, became confused, resistive and had to be forcibly fed. He was doubly incontinent. Eventually he had to be kept in bed. He could rarely be induced to speak and then only in a very soft voice. He looked utterly miserable, frightened and apprehensive.

For two days after operation he was a little more cheerful and interested, but soon relapsed into his former depression and agitation. He was also frequently doubly incontinent by night. He has remained depressed, retarded, apprehensive, intermittently restless and agitated, with no constructive activities, and in him the effect of operation was extremely small, and distinctly less than in the schizophrenics.

CASE 17.

This was the patient with chronic agitated depression who died three months after operation. The onset was apparently gradual with loss of memory, slowness, and difficulty in thinking clearly and soon in doing her ordinary household tasks. She then developed into a deep depression. Six courses of E.C.T. failed to produce more than the most transient improvement and in fact, apart from a few days of remission, she remained profoundly depressed for the next three years. Often she was tense and agitated, and would moan loudly and distressingly. Sometimes she could not be made to reply at all and she would mutter incoherently under her breath. This patient was seen also by Dr. Eliot Slater, who considered it important to try the cingulate operation on such a patient.

After operation she was little different, though she spoke in a fuller voice. Three weeks later she was given E.C.T. with curare. Within a day or two it was noticed that she was inclined to fall forward, and she did fall and cut her forehead. She then developed head retraction, refused to eat, and was doubly incontinent. She had one epileptic fit, during electroencephalography, a month after operation. She was found to have a low-grade meningitis. A small collection of pus, films of which yielded only Gram-positive cocci, was found in the bed of the cingulate ablation. This infection was cleared up by aspiration and instillation of penicillin, but she developed bronchopneumonia and died.

Results.

Broadly, the results are that no patient has been discharged from hospital and there has been no example of the kind of dramatic improvement which sometimes follows full frontal leucotomy ; nor has it been possible to upgrade patients permanently to a better ward, though it has been possible temporarily. But while there has been but negligible relief from suffering, the patient has never been worse off. There has invariably been a period of post-operative improvement. However bearing in mind the expected variability in the disease, the relatively short time since operation in illnesses with a life-long course, and the expected effects of general interruption of routine and the submission to operation of any kind, one can only conclude that over a long term the patients are psychiatrically and socially unaltered.

There has, then, been no effect on the whole course of the illness ; though the temporary improvement while it lasted was both definite and therapeutically useful. It made possible a relaxation of the nursing attention ; patients were more amenable to help and discipline and fitted in more smoothly with the routine planned for them. Five severely hallucinated patients, in whom sleep was always disturbed, slept better. Three continued to sleep well without hypnotics for up to a year.

Eleven patients have at some time shown some improvement after operation. The remainder have not changed : to be accurate, they have exhibited slight changes which, because of their nature, raised the possibility that they were sequels of operation ; but they could not unequivocally be distinguished from the minor fluctuations naturally occurring in the course of these illnesses.

In the eleven patients who took a turn for the better and who showed promise of good recovery, the improvement soon proved to be short-lived. Within a few weeks, varying a little from patient to patient, they all relapsed. In one, whose gradual remission was delayed, some degree of overall improvement has been maintained. In some in whom there was a symptomatic improvement for longer than the overall temporary improvement, it consisted of some amelioration of conduct so that they were less violent, less suddenly impulsive or less erratic and unpredictable.

This is reflected in the reduction in the use of sedative drugs, which were greatly reduced or even stopped during the remission. As relapse began, sedation was again necessary, but smaller doses of drugs were usually sufficient. While pre-operatively three patients were on very heavy doses, three on heavy, and four on moderate doses, now only one is on very heavy doses, and four require none. Here we refer to constant use of drugs, a very heavy dosage being perhaps 9 grains of sodium amytal together with 4 drachms of paraldehyde daily; a moderate dosage 3 grains of phenobarbitone daily.

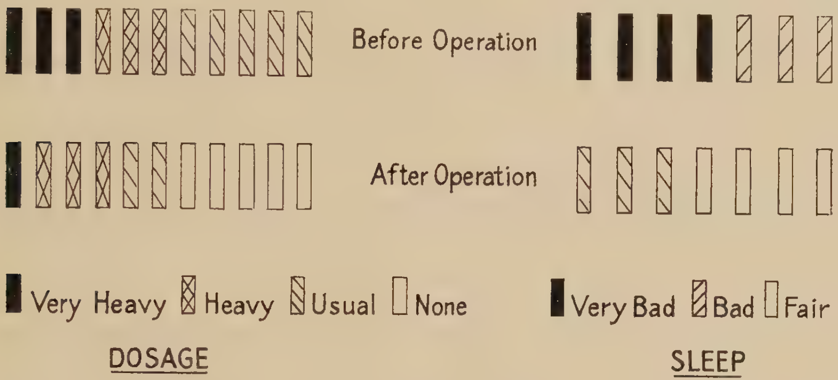

FIG. 2.—Effect of operation on the necessity for heavy doses of sedative drugs (11 patients) and on sleep (7 patients).

The only other change which remains is an increase in appetite. There are 10 patients with increased appetite, and in four it is marked.

Type of Change.

Typically the patient entered a phase of quieter and more rational behaviour soon after operation, the effect being clearly established after about a month. This state persisted for two to eight months. In two it lasted two months; in three, three months; in four, four months; in one, eight months; and in one, for very much longer.

The largest single factor which accounts for this improvement is the relief of tension, or, as was more apparent in some cases, a loss of subjective anxiety or apprehension. This was one of the observations which led to the trial of the operation in certain psychoneurotics (Macdonald Tow and Whitty, 1953). The second factor is an alteration in the affective aspects of behaviour resulting in less aggressive, less impulsive, and less erratic and irrational conduct.

The chronic hallucinated schizophrenic with impulsive aggressiveness is the type of patient who has most clearly shown this temporary remission; but beyond this emphasis, which is a rather tenuous one with this material, there is *no* correlation between type or severity of schizophrenic illness and the amount of improvement. Nor did the age of the patient influence the result, for of the nine improved patients there were: three below 30, three between 30 and 40, three over 40. One over 50 and the two over 60 who failed to change were the two agitated depressives and the presenile dement. Similarly the duration of the existing illness was not relevant: of the eight who had been ill more than 10 years, six improved; of nine who had been ill for less than 10 years, four improved.

Summarizing the relevant data in the histories there are: six patients who were generally better behaved and better tempered, seven who seemed less tense and apprehensive, seven who had the sharp edge taken off their violence (including two who were distinctly less purposive and directed in their outbursts) and five who were in better contact with reality. These were the primary clinical impressions and as such may help to convey briefly the behavioural changes we have observed.

Complications.

The only somatic complications have been epilepsy and incontinence; neither has been persistent. If a therapeutic use is found for the operation they would not appear to be serious sequelae. Only in one case have fits persisted: patient 2, the schizophrenic, who had in fact had one isolated fit before cingulectomy, has had 12 fits spread over the post-operative two-and-a-half years, the first occurring after nine months. Patient 11 had seven fits on the second day. Patient 3 had 12 fits at two weeks post-operatively but it is noteworthy that she probably had fits in adolescence. Neither of these have had more fits.

The fourth patient to have a major epileptic attack was the one fatal case. She had one isolated attack a month after operation; while already ill with meningitis, and during her electroencephalographic examination.

Though twelve patients have been incontinent of urine and three of faeces, this has invariably been a transient phenomenon, often only in the first week. Three had been incontinent before operation and analysis shows that there was no really persisting incontinence in those not incontinent before. The worst individual case was a woman who was incontinent of urine and faeces for the first two months.

It is of interest, though not surprising, that in two deteriorated schizophrenics who were doubly incontinent before operation, incontinence after operation ran closely parallel with the psychiatric state. Immediately after cingulectomy when they were clinically better, there was very little; for the next three months, when they were psychologically at their best, there was no incontinence; then, with a clinical deterioration towards their former state, the old double incontinence gradually returned. This could, of course, also be regarded as contributory evidence of the marked temporary improvement.

About three months after operation, the clinical improvement in the group as a whole was at its maximum; it then receded. This has resemblance to the effect in monkeys. In them there was a loss of sense of danger, loss of anxiety and of fear of man, avoid approach to food and a marked restlessness. So far as we can make comparison, the effects reproduced in the aggressive psychotics represent the same sort of emotional changes, and are comparable; they are quieter, generally more manageable, and less aggressive; and sometimes, such as in the patient who asked for lipstick for the first time soon after operation, the changes are certainly marked; they may lose their apprehensive facies and attitude, their fear, or their anxious hypochondriasis. In both the changes are short-lived.

SUMMARY.

We report the effect of bilateral anterior cingulectomy on chronic psychotic illness, mostly schizophrenic. There is a temporary overall improvement ; it lasts three months with an occasional amelioration of conduct persisting for up to 18 months.

Two cases of agitated psychotic depression did not respond.

As the lesions were in all cases confined to the anterior half of the cingular gyrus, it is of interest to note the resemblance to the effect of a similar lesion in monkeys : the data may be of interest physiologically.

No lasting or therapeutically valuable improvement occurs. One patient died. Somatic complications were epilepsy and incontinence : neither was serious.

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LEUCOTOMY—A RECENT DEVELOPMENT.*

By Harvey Jackson, F.R.C.S.

In 1947 the Board of Control published its report on the results of 1,000 leucotomies, citing therein a mortality of 6 per cent. Five years later Dr. W. S. Maclay, in his Presidential Address to the Section of Psychiatry of the Royal Society of Medicine, referred to 180 deaths during the interval, a mortality of approximately 2 per cent. Although this is a striking improvement there is still cause for apprehension, for by far the greatest proportion of fatalities arise out of haemorrhage. The second causative factor in fatal issues is infection. Something must be done to put psycho-surgery on a yet safer basis.

When originally I undertook to perform leucotomy it was not without a feeling rather of reproach, for mutilation no doubt it must be. However I first of all went to watch my psychiatrist colleagues applying chemical or electric convulsive therapy—so disturbing was the exhibition at that time that thereupon I decided that the surgical approach was possibly a less traumatic measure. One's earlier experiences, of course, were based on chronic institutional patients, many of whom had had much previous treatment often including recurring series of convulsive treatments. Many if not most of the patients had proven intractable to all other forms of treatment, consequently any prospect of a return to normal social life was poor indeed, if not lacking completely. Working on such material meant that one encountered some patients with quite gross atrophic changes in the brain. As no such shrinkage was related to mental disease, on the submission of the psychiatrists of the institution, it led me to seek an explanation in treatment. The more experience one has gained the more does one feel that electro-convulsive therapy has been responsible for much atrophic change, possibly arising out of repeated diffuse petechial haemorrhages.

At that time the requirements of leucotomy were best described by Freeman and Watts, and it was a modification of their technique that one put into practice. Results were encouraging in selected cases and a series of cases accumulated that showed promise, at times remarkable. During the course of this early series a case of haemorrhage occurred, requiring the reflection of a bone flap in order to expose the vessel and control the bleeding. It was then that a full appreciation of what should be required of any surgeon who undertakes leucotomy was realised : he must have had neurosurgical training if he is to be capable of dealing with the complications with which he may be faced. One should realise that haemorrhage arising out of leucotomy may even require resection of the frontal pole of the brain in order to expose the damaged vessel. Increasing experience brought one into contact with other psychiatrists and other mental establishments. In some of these institutions a new problem presented—that of being invited to operate under conditions upon which even old-fashioned back-room boys would have frowned. Herein rests one of our present difficulties—what should one undertake where no satisfactory accommodation for surgical operations is available ? Not infrequently I have met the comment " Mr. So-and-So has operated here a number of times." Leucotomy, like any other surgical procedure should not be undertaken unless proper hygienic precautions are possible, and the apparatus necessary to neurosurgery is at hand. Only by taking such precautions are we to avoid that second disaster, sepsis.

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* A paper read at the Quarterly meeting of the Royal Medico-Psychological Association, at 11, Chandos Street, W.1, February, 1953.

We must ask ourselves seriously why so many different forms of surgical intervention avail ; e.g., Topectomy, Cortical Undercutting, Thalamotomy, Cingulectomy. Have these various methods any factor common to all ? The aim of surgery surely is to disrupt such connecting pathways as relay impulses inducing the individual's response to his thoughts. It appears that interruption in fronto-thalamic pathways is an anatomical requirement of operation. Of the different methods applicable it seems to me that leucotomy is the simplest procedure of all ; less cerebral damage arises out of it, the risks of complications are less, post-operative epilepsy is less frequent, and it appears improbable that any of the other methods has anything better to offer in terms of functional (physiological) effects. From controlled section I have yet to see intellectual deterioration.

During the course of observation of many cases one has been struck by certain side effects of operation : changes in blood pressure, in prominence of the eyes, in respiration. A grossly enlarged thyroid in a seriously depressed patient shrank under vision, and an uncontrollable diabetes became controllable. These effects together with other forms of response rather suggest that leucotomy may well do something other than produce an undoubted quelling of nervous tension. The work of Fulton and others has drawn attention to the import of the frontal cortex overlying the orbital roof in relation to autonomic control, and later of course to the function of the cingulate gyrus. One has gained the impression therefore that the important and effective part of frontal leucotomy is related mainly to division of white matter in the lower and mesial segment.

Whereas I had carried out many leucotomies aimed at division of the greater extent of frontal white matter, the early cases were generally chronic psychotics who had failed to respond to other forms of treatment or who had made some improvement which had not persisted, and one worked under a certain degree of apprehension lest damage should occur leading to apathetic, blunted, detached or inaccessible patients. As one gained in experience it became reasonable to offer the benefits of leucotomy to rather different types of individuals. These cases have not been the same chronic incurables ; moreover persons of good intellect have been involved. The risk then of dulling or deterioration has caused one even more concern. The technique of the operation involved will be described.

The Author's Method of Performing Leucotomy.

The incision in the scalp is made in the line of the coronal suture after the manner of Freeman and Watts. Division of tissue is carried to the bone and a self-retaining retractor introduced. A cranial defect of three-quarters to one inch in diameter is fashioned with a trephine centred at a point six centimetres above the upper border of the zygoma. The disc of bone excised is retained in sterile warm saline, pending replacement.

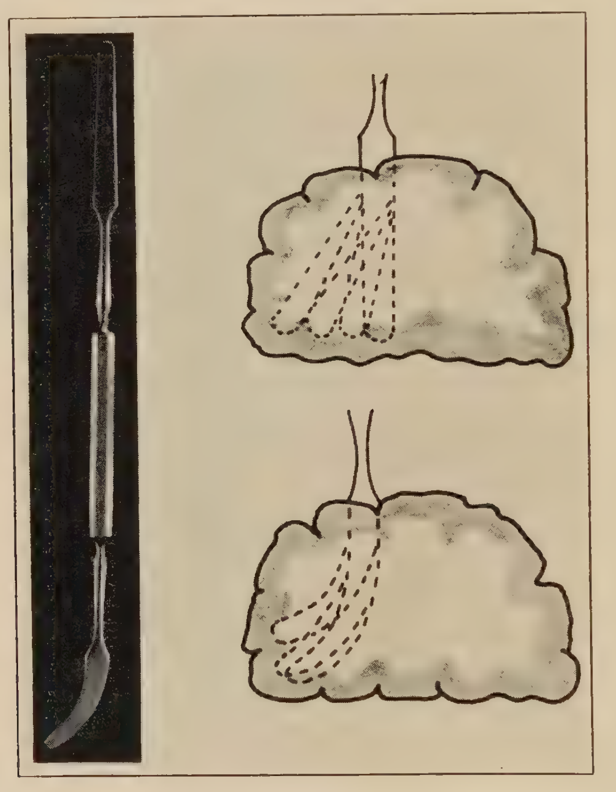

Diagram to show how the leucotome is applied.
The author's leucotome.

Bleeding from the dura-mater duly controlled by diathermy, a V-shaped incision is made in that membrane permitting reflection of a small triangular flap.

A site on the cortex is selected, small overlying blood vessels are coagulated, then a short incision (about 0·75 cm.) is made. Through the incision a brain cannula is inserted and directed towards a like point on the opposite side of the head. By encountering the lateral ventricle in this or subsequent insertions, the position of the anterior horn is determined. Likewise by suitable direction of the cannula downwards and inwards, the margin of the lesser wing of the sphenoid is detected. Thickness of the cerebral white matter is assessed by measurement of the distance between the surface wound and the falx after making due allowance for the width of the cortex traversed. With these data the plane of the proposed section is selected and is registered by a straight instrument retained by an assistant in apposition with the surface of the head during succeeding manoeuvres.

On account of restricted exposure and the desire for curtailment of cortical damage a double ended leucotome is required, one blade straight, the other curved.

Division of white matter is not made with a sweeping action but by a series of stabs with the straight blade applied at varying angles from the horizontal, followed by the curved blade in a requisite number of movements applied in the long axis of the blade. No greater pressure is applied than the weight of the instrument held between the thumb and index finger. By this simple manoeuvre the resistance on engaging a blood vessel is easily appreciated and a slight deviation in the course of the blade permits circumnavigation of the vessel.

On completion of the section a forceful stream of warm saline is thrust at the cortical opening—the lips of the incision are separated thereby and staining of escaping fluid reveals the degree of haemorrhage, if any.

All bleeding controlled, the dural flap is replaced, then retained by a suture. The disc of bone is then replaced and the overlying wound closed in layers.

HEMISPHERECTOMY.*

By H. H. Fleischhacker, M.D.,

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I. Introduction.

Hemispherectomy in man† (ablation of the cortex, the underlying white matter and nucleus lentiformis) was performed first by Dandy (1928, 1933), later by Gardner (1939) and a few others, on adult patients suffering from large infiltrating tumours of the subdominant hemisphere, with one exception (Zollinger, 1935). It was carried out by McKenzie (1939) apparently on a patient suffering from infantile hemiplegia with epilepsy. Krynauw (1950*a*, *b*) began systematic work of this nature on cases of infantile hemiplegia with epilepsy and personality disturbances. Apart from its therapeutic value, in carefully selected infantile hemiplegics, in the hope of lessening or curing epilepsy, and exerting a beneficial influence on behaviour and further mental development, the comparatively small loss of functions after removal of one hemisphere is most remarkable.

I hope to demonstrate this in five patients. In the paper following I shall try to show how one may understand, in principle at least, these amazing results. During the demonstration I shall touch on some aspects concerning the single patient, and it will become clear how much work has still to be done in order to comprehend the problems of, and do justice to, each individual patient. Some of these problems will be mentioned as far as they are relevant to the main theme. Problems not mentioned may yet turn out to be just as important as those mentioned ; but their importance may not be appreciated by the present author.

II. Findings (Case Demonstration).

The five patients (all of Harperbury Hospital) operated on by hemispherectomy at the National Hospital, Queen Square (Mr. W. McKissock), had and have all some common and some individual features before and after operation. They are all sufferers from infantile hemiplegia with fairly low-grade mental deficiency. They all had epilepsy and personality disturbances before operation. From the operation they have all, with one exception (J. M—), benefited one way or the other, and none of them is mentally or physically worse after it, including J. M—.* Individually, they all offer mental and physical differences pre- and post-operatively, as can be seen from the case papers. Although, in this demonstration I am dealing essentially with the "non-psychological" aspect of the matter, I have at the end of each case paper given a few "mental" characteristics of the patient. The short statements on the cerebral pathological findings I owe to the kindness of Dr. Mair, and on the pre- and post-operative E.E.G.s to Dr. W. Cobb (through Dr. J. Bates), all of them at the National Hospital, Queen Square, London.

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* Case demonstration and paper read at the Annual General Meeting of the Mental Deficiency Section of the R.M.P.A. (Harperbury Hospital), 1 May, 1953.

† In monkeys, the first systematic studies were made by Karplus and Kreidl (1914), the most accurate description of the consequences of hemispherectomy in apes is by Fulton *et al.* (1938, 1949).

From the anatomical-pathological point of view these five patients fall into two groups. Two (D. G— and V. R—) had cysts in the distribution of the middle cerebral artery ; the other three had more diffuse processes (A. L—, A. Z— and J. M—). For reasons which will become obvious later, the clinical findings have been written up in a somewhat unorthodox way.

All patients can speak, dress, are more or less well orientated in time and place and have no disturbance of the body image, irrespective of whether their r. or l. hemisphere has been removed. They all can hear equally well in both ears, there is no ataxia or gross disturbance of co-ordination. None of them shows forced grasping, forced circling, etc. They are all hemianoptic. The sense of smell could not be assessed very well, but it is to be presumed that they have lost it on the side of the operation. Having pointed more or less to what is common to them I want now to stress a few points in which they differ individually.

CASE PAPERS.

A. L—. Date of birth : 12.iii.38. Operation : 19.i.50. First seen and treated at Shenley : 16.xi.50.

A right-sided hemiplegia (fairly typically spastic now, essentially athetoid before operation). Still a number of epileptic fits.

I. *Physical Functions.*

A. *Essentially bilateral central innervation :*

(i) *Motor :* Upper VII, r. somewhat worse than l. V_3 : r = l. ; eye movements : free.
Speech : Somewhat bellowing. Muscles of neck and trunk : r. = l.

(ii) *Sensation :* Epicritic : touch possibly less well felt and localized on r. ; protopathic : frightened of the needle.

(iii) *Co-ordination :* Slight nystagmus ; more to the left (barbiturates) ; otherwise good.

(iv) *Vegetative :* Temperature of skin : r. = l.

B. *Essentially unilateral central innervation :*

Face : R. lower VII slightly worse than left. Tongue : midline ; visual fields : r. hemianopia.

Limbs :

(i) *Motor :* R. arm and leg fairly typical spastic paresis, without contractures of arms, but of foot. Movements of wrist and fingers practically impossible. Fingers fairly flaccid, but spastic on extreme movements, and throughout when wrist is brought up to horizontal. Wrist clonus at times, no forced grasping.

(ii) *Sensation :* Epicritic : localization of touch not very good, finer examination impossible.

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* They owe a great deal of their rehabilitation to Miss E. Bagley, the late, and Miss K. Rattray, the present Physiotherapist to Shenley Hospital.

(iii) *Co-ordination :* F.N.T. : normal. Diadochokinesis : r. impossible. On left (!) slight dysdiadochokinesis.

(iv) *Vegetative :* Temperature slightly colder right than left (fairly warm weather). Trophic : v. slight atrophy. Abd. refl. r. less than l.

Change after training : joints freed ; mass-movements of arm broken up somewhat into more isolated movements of large joints.

II. *Non-Physical Functions.*

A. *Essentially unilaterally innervated :*

(i) " Absolutely " dominant. Speech : bad, originally only telegram style ; now begins to speak short but full sentences. Three R's impossible. Praxia for objects and " concrete " construction good. " Symbolic " constructive praxia bad, cannot draw. Some dyspraxia of right shoulder movements and possibly of diadochokinesis.

(ii) " Relatively " dominant : functions of body scheme (sensory and motor) : good.

B. *Essentially bilaterally innervated (" co-dominant functions ").*

Orientation in place : good ; in time : worse (the latter most likely a consequence of low grade M.D.).

Behaviour in Shenley : A noisy, affectionate, easily contented boy who gives very little trouble. Before operation : ill-mannered, dirty, voracious, some attempts at running away, stubborn, occasionally aggressive when thwarted. Apprehensive, not shy.

Path. Anatomy.

Numerous gliosed lesions of the cortex and white matter scattered throughout the hemisphere. In these scarred regions the nerve cells and axons had disappeared.

E.E.G.

19.xii.49. Bad record. No alpha. Irregular low voltage slow background with some larger 4 c./s., a little better seen on right. Asymmetry slight.

Left hemispherectomy 19.i.50.

3.iii.50. Considerable increase in right-sided alpha. Other activity about the same. Flat on left.

2.x.50. Left flat. Right ? normal for age with good alpha and some 3–7 c./s.

31.x.50. Restless—bad record. Some slower waves on right—? sleep. No P.C. with flicker—useless.

6.ii.51. (1) Artefacts, but flicker is fair at times and becomes more nearly symmetrical at higher frequencies (in occipital channels only).

6.ii.51. (2) Better. Slow waves, around 6 c./s. are surely more than normal for 13 years, but slower waves came up only on drowsiness from 6 gr. seconal. Fast activity not great but definite.

4.ii.52. Restless and unco-operative. Very poor record. Slow activity seems larger and more persistent than before, but this may be artefact.

10.i.53. Left flat. Right small irregular alpha and low voltage 4–7 c./s. with slower waves. 6 gr. seconal not very effective.

D. G—. Date of birth : 12.ii.1927. Operation : 16.viii.50. First seen at Shenley and treated : 29.xi.50.

A left-sided infantile hemiplegia with contractures of all joints of arm and v. slightly of foot. Still had epileptic attacks until about one year ago.

I. *Physical Functions.*

A. *Essentially bilateral central innervation :*

(i) *Motor :* Lower VII, V3, speech, neck, trunk : good (r. = l.). Eye movements : slight paresis of l. internus and rectus superior. No double vision.

(ii) *Sensation :* Epicritic : face : r. = l. (including localization of touch) ; localization on trunk l. a little worse than r. Protopathic r. = l.

(iii) *Visual fields :* L. hemianopia.
(iv) *Co-ordination :* Eyes : slight nystagmus, more to r. otherwise good (no barbiturates). Trunk : good.
(v) *Vegetative :* Temperature of skin r. = l.

B. *Essentially unilateral central innervation :*

I. *Motor :*

(a) *Face :* Lower VII l. trace worse than r. Tongue slightly to r. Slight diadochokinesis of tongue (l. frontal lobe damaged).

(b) (i) *Arm :* Contractures increasingly towards wrist, but not of fingers ; mobility of shoulder and elbow hampered by a slight spasticity, while wrist and fingers are unusually flaccid. Power in shoulder and elbow quite good. Wrist only very slight movements ; fingers : no isolated movements. Can grip and hold slightly. Thumb : extension very bad ; opposition and adduction better. Extension of other fingers slight ; flexion and opposition of five practically *nil* (demonstration). *Changes after training :* Original stiffness of all joints overcome ; mass movements of whole limb broken up into more isolated movements of individual joints. The possible movements can be carried out fairly quickly.

(ii) *Sensation :* Epicritic of hand fairly bad in every respect. Protopathic : l. about r.

(iii) *Co-ordination :* F.N.T.: r. = l. Diadochokinesis : l. impossible ; r. good.

(iv) *Vegetative :* Temperature of skin : r. = l. (in warm weather : somewhat worse in colder weather). Trophic : l. arm : about 2½ in. shorter.

(c) *Abdominal reflexes :* Cannot be tested ; too ticklish.

(d) *Leg :*

(i) *Motor :* Slight spastic paresis of l. leg with spastic reflexes. Foot : only slight plantar and very incomplete, dorso-flexion : toe movements better : No diadochokinesis possible (? also not quite good on r.). K. H. T. r. = l.

(ii) *Sensation :* No detailed examination possible.

(iii) *Co-ordination :* Good.

(iv) *Vegetative :* Temperature of skin as arm. Trophic : slight atrophy.

II. *Non-physical Functions.*

A. *Essentially unilaterally innervated :*

(i) "*Absolutely*" *dominant :* Speech good. Three R's not possible. Praxia good. Refuses to draw, etc.

(ii) "*Relatively*" *dominant :* Functions (motor and sensory) of body scheme good.

B. *Essentially bilaterally innervated.* ("*Co-dominance*) :

Orientation in place and time good. Knows usually r. from l.

Changes after operation : Has learnt to count up to 10. Behaviour at Shenley: Very touchy but ambitious (for time being) ; treatment had to be interrupted for two years as he refused to co-operate. Before operation, shy, solitary, moody, aggressive, anti-social, morose, window-breaker.

Anatomy : Presented a cyst in the distribution of the middle cerebral artery.

E.E.G. :

2.viii.50. Definite right-sided abnormality, but amplitude not great. Mainly 4 c./s. waves, some slower. Sharp waves in parieto-temporal region. Dubious silence in temporal.

15.viii.50. Asymmetry less obvious. After seconal minute fast rhythm in left frontal.

Right hemispherectomy 16.viii.50 temporo-parietal cyst.

24.viii.50. Poor record : nothing new on left. Right flat but lot of artefacts. Bilateral rhythms with common electrodes.

7.ix.50. Alpha rhythm 7–8 c./s., some slow waves on left. Quite a lot on right, but only near midline. Trivial asymmetric fast response to Seconal.
28.ix.50. Slow alpha of better amplitude, but slower waves less apparent. Still quite a lot of right-sided activity, mainly near midline which sometimes seems indepedent in frequency and amplitude.
18.x.50. Similar.
28.iii.51. Slightly different from last. Dominant 6–8 c./s. blocked by visual attention mixed with 4–7 c./s. On right seems some irregular low voltage. *Flicker :* Small, equally seen on both sides. Seconal : Some fast on left.
13.ii.52. Unchanged from last.
9.xii.52. Unchanged from last.

V. R—. Date of birth : 8.ii.1929. Operation 23.xi.50. First examined and treated at Shenley 2.iv.51.

A right-sided infantile hemiplegia with epileptic equivalents (about two or three times a month) after operation, and before operation, many epileptic fits. Contracture of shoulder and wrist ; wrist somewhat corrected by orthopaedic operation about one and a half years ago.

I. *Physical Functions.*

A. *Essentially bilateral central innervation :*

- (i) *Motor :* Upper VII, r. = l. V.3. r. = l. Eye movements free. Muscles of neck and trunk r. = l. Speech : somewhat slow ; improving.
- (ii) *Sensation :* Epicritic (including localization) and protopathic ; slightly disturbed after operation, slowly recovering, now r. = l.
- (iii) *Co-ordination :* Eyes : slight nystagmus to l. (no barbiturates). No ataxia. (R. frontal pole damaged.)
- (iv) *Vegetative :* Temperature of skin : r. = l.

B. *Essentially unilateral central innervation :*

- (a) *Face :* Lower VII : r. slightly less than l. Tongue : v. slightly to r. Diadochokinesis of tongue : Good. Visual fields : r. hemianopsia.
- (b) *Arm :*
  - (i) *Motor :* Mixture of spasticity and rigidity (varying in degree) in shoulder and elbow. Wrist : Surgically stiffened (arthrodesis in mid-position). Fingers flaccid, but spastic in extension on quick stimulation (stretch). Power in larger joints good. Closing of fist fairly good. (diminished immediately after operation.) Thumb extension slight, opposition, better, Despite flaccidity can use hand for holding and grasping (demonstration). No forced grasping. Very much improved after training. Can carry out very quick movements.
  - (ii) *Sensation :* Epicritic ; cottonwool, bilateral touches : r. = l. Two point discrimination, joint sense for finest movements, recognition of surface structure, stereognosis less good than l., but improving under training (demonstration). Protopathic : r. = l. (also 2-point discrimination for pain).
  - (iii) *Co-ordination :* No ataxia. Diadochokinesis of fingers good.
  - (iv) *Vegetative :* Trophic : slight atrophy. Temperature of skin : r. slightly colder than l.
- (c) *Abdominal reflexes :* R. slightly less than l.
- (d) *Leg :*
  - (i) *Motor :* Slight spastic paresis r. On left : occasionally very slight spasticity of knee and ankle, toe fanning, Mendel-Bechterew, Rossolimo (? already present before operation).
  - (ii) *Sensation :* Epicritic, including joint sense, and protopathic good, not much difference between r. and l.
  - (iii) *Co-ordination :* Good.
  - (iv) *Vegetative :* Slight r. atrophy. Temperature of skin : r. slightly colder than l.

II. *Non-physical Functions :*

A. *Essentially unilateral innervation :*

(i) " *Absolute* " *dominance :* Speech good ; reading, writing slowly improving. Arithmetic bad. Thinking : Not too good. No apraxia for objects or construction, can draw. Speech quicker after operation.

(ii) " *Relative* " *dominance :* Functions of body scheme (motor and sensory) good.

B. *Essentially bilateral innervation* (" *Co-dominance* "):

Orientation in place and time (can read clock), and r. and l. differentiation good.

Behaviour at Shenley : At times somewhat moody and slightly fatuous (usually before and after epileptic equivalent). Usually even tempered, fairly ambitious, very reliable, no trouble. A few years before operation he had, on slight provocation, attacks of violence with window-breaking, according to him, only when provoked.

Anatomy :

A cyst in the distribution of the middle cerebral artery.

E.E.G. :

Pre-operative : (4 records) right some alpha and much 3–7 c./s. Left flat in frontal and parietal. Posterior temporal focus of slow waves with spikes and sharp waves. Flattening not confirmed by seconal and sleep.

Post-operative : (5 records) on right at first similar to pre-operative, but becoming more normal. Now very nearly normal.

A. Z—. Date of birth : 10.iv.38. First seen 27.i.51. Operation : 7.iii.51. Treatment started at Shenley 12.v.51.

Left infantile hemiplegia. Epilepsy : cured (so far).

I. *Physical Functions.*

A. *Essentially bilateral central innervation :*

Motor : Lower VII, V3, eye movements, neck, trunk : good, unchanged after operation.

Sensation : Epicritic and protopathic of face, neck and trunk : practically normal, even localization of touch, unchanged after operation.

Hearing : Good, unchanged.

Co-ordination : Eye, neck and trunk movements : essentially unchanged ; normal.

Vegetative : Temperature of skin r. = l.

B. *Essentially unilateral central innervation :*

Face : Lower VII, left trace less than right (unchanged).

Visual fields : ? Left hemianopia before, definite hemianopia after operation.

Arm and Leg :

(i) *Motor :* Main characteristics : no contracture of arm or leg (except tenotomy of left foot 1948). Mobility of large joints almost normal. Power decreasing peripherally, practically *nil* in wrist, poor in foot. No isolated finger movements, some opening and closing of hand. Holding of objects somewhat favoured by rigidity, particularly thumb and next two lateral fingers (demonstration). Tonus of muscles of large joints : fairly free, but variable in elbow. Wrist fairly stiff. Neurological changes after operation : slight increase of tonus in wrist, fingers and elbow. No forced grasping. Changes by training : movements of fingers somewhat better ; some improvement in use of hand for grasping and holding (demonstration).

(ii) *Sensation :* Normal before operation. After operation, slight disturbance of localization and discrimination for touch (demonstration).

(iii) *Co-ordination :* No ataxia. Diadochokinesis of hand on left impossible, not too good in elbow and thumb ; on r. not always quite good (? dyspraxia).

(iv) *Vegetative :* Temperature of limbs : not tested before operation. Now left limbs much colder than right. Moderate atrophy of arm, slighter of leg (not much change).

II. *Non-physical Functions.*

A. *Essentially unilateral innervation :*

(i) *"Absolute" dominance :* Speech and Praxia : good. Three R's not possible, cannot draw. Thinking bad. Speech : stuttering pre-operative.

(ii) *"Relative" dominance :* Functions of body scheme : good.

B. *Essentially bilateral innervation* (*"co-dominance"*) :

Orientation for place good ; time : bad. R. and l. differentiation : bad.

Changes after operation : none .

Behaviour at Shenley : Very difficult. Jealous, hypersensitive, stubborn, spiteful and resistive when he has not his own way. Before operation these trends were still more outspoken, with frequent outbursts of the most violent aggression. He was frightened of epileptic fits.

Anatomy :

Most of the gyri appeared normal. The gyri in the island of Reil were small and gliosed.

E.E.G. :

Always difficult, and most records are in seconal sleep.

Pre-operative : (l. record) very pronounced asymmetry of fast rhythm, absent from r. side. On left 6 c./s. and slower waves, depending on depth of sleep. In right frontal, runs of very slow waves with spike or sharp wave.

Post-operative : (4 records) flat on right, less slow and some alpha on left and probably normal sleep responses.

J. M—. Date of birth : 23.iv.39. First examined : 1.ii.51. Operation : 12.iii.51. Treatment started at Shenley : 21.v.51.

Right-sided infantile hemiplegia, with slight total facial weakness on right, and also very slight pyramidal-lesion on left before operation. Still a number of epileptic fits.

I. *Physical Functions.*

A. *Essentially bilateral central innervation :*

(i) *Motor :* Upper VII r. less than l. (weakness very pronounced after operation ; now as before). V3 r. = l. Eye movements : free ; speech: no dysarthria. Muscles of neck and trunk, r. = l.

(ii) *Sensation :* Epicritic and protopathic : r. = l.
(iii) *Co-ordination :* No nystagmus, no ataxia.
(iv) *Vegetative :* Skin temperature : r. = l.
} No change.

B. *Essentially unilateral central innervation :*

(a) *Face :* Slight weakness of lower VII on r. After operation worse ; now as before.

Visual Fields : Full before operation, now r. hemianopia.

(b) *Arm :*

(i) *Motor :* Fairly typical hemiplegia with a mixture of changing rigidity and spasticity in shoulder and elbow (contracture of elbow for supination), and of wrist. Wrist and fingers at times hypotonic, at times spastic ; particularly thumb and radial fingers. Movements of arm poor ; usually only a mass movement in shoulder possible ; at times slight flexion in elbow if he understands what one wants. After operation : worse. After treatment : original stiffness of shoulder much lessened, otherwise not much progress ; attends treatment very irregularly, due to frequent epileptic attacks.

(ii) *Sensation :* Epicritic : satisfactory before operation, now disturbance of localization for touch. Protopathic : apparently r. = l. no change.

(iii) *Co-ordination :* No ataxia. Diadochokinesis : not possible on right. On left dysdiadichokinesis elbow and thumb.

(iv) *Vegetative :* Atrophy r. arm. Skin temperature r. = l, (at average room temperature).

(c) *Abdominal reflexes :* r. = l. before operation ; now r. less than left.
(d) *Leg :*
- (i) *Motor :* Moderately severe spastic paresis r., with usually more flaccid contracture of foot, and spastic reflexes and spastic gait. Very bad after operation, now about as good as before, possibly with the exception that the slight foot movements, present before operation, are absent now (but he scarcely makes any attempts at movements). Very slight spasticity on l. with some spastic reflexes.
- (ii) *Sensation :* About r. = l. ; apparently little change ; finer examination impossible.
- (iii) *Co-ordination :* No gross disturbance (unchanged).
- (iv) *Vegetative :* Skin temperature : r. foot usually colder. Trophic : r. leg atrophic, but less so than arm.

II. *Non-physical Functions.*

A. *Essentially unilateral innervation :*

(i) *"Absolute dominance" :* Speech and praxia : no gross disturbance ; 3 R's, drawing impossible. Thinking : very poor. No change.
(ii) *" Relative " dominance :* Functions (motor and sensory) of body scheme : no gross disturbance. No change.

B. *Essentially bilateral innervation* (" *co-dominance* ")*:*

Orientation for place not grossly disturbed, for time bad, r. and l. differentiation impossible. Unchanged.

Behaviour at Shenley : Not very interested in training ; very playful but no trouble. At Harperbury, before and after operation : moody, solitary, aggressive towards patients and staff ; occasionally a window-breaker.

Anatomy :

Extensive damage mainly in the fronto-parietal region where loss of nerve cells and myelin, and glial scar formation had taken place.

E.E.G. :

13.ii.51. Lack of co-operation necessitated use of seconal and record commenced a quarter of an hour after 3 gr. Asymmetry was slight at first, but quickly increased as the patient became drowsy and slow activity at first around 4 c./s. appeared on the right side together with transients suggesting slow spike and wave complexes. As sleep deepened this activity became much more pronounced and frequently constituted an arousal reaction. Photic stimulation did not show any convincing differences and the response was small. Left hemispherectomy 12.iii.51. Fronto-parietal blood clot.

5.iv.51. Patient more co-operative. Record obtained without seconal, but not perfect. Relatively flat on both sides, anteriorly, but alpha rhythm posteriorly best seen in *left* occipital channels, i.e., those with one electrode on the occiput. Some irregular low voltage slow activity on the right side. Photic stimulation again inconclusive. Probably normal.

27.iv.51. Six gr. seconal. No sleep nor increase in fast rhythm. Right side not different from 13.ii.51 before sleep. Left side flat.

11.xii.51. Awake. Good alpha rhythm. Right frontal occasional single sharp waves, but on one occasion repeated regularly. Generalized low voltage slow and in the occipito-temporal region focus of $1\frac{1}{2}$–2 c./s. waves occurring in long regular bursts.

24.i.52 : Further increase in slow activity and in frontal sharp waves which tend to occur in episodes at 2 c./s. for about 10 sec. Arise far forward on right and constant in site.

3.xii.52. Awake, left flat. Right low voltage alpha, some fast, some theta, occasional small sharp waves. Asleep : long runs of right frontal 2 c./s. spike and wave complexes, spreading and slowing in deeper sleep.

INDIVIDUAL DIFFERENCES.

A. *Motor and Vegetative Functions.*

I. *The Cystic Patients (D. G— and V. R—) both with Pre-operative Damage to the Remaining Frontal Poles.*

Both have contractures in the upper limb, the fingers of both are very flaccid, but V. R—on very quick passive extension of the fingers shows spasticity, D. G— does not. While the eye-movements of both are quick into the hemianoptic visual field, V. R—'s eye-movements are free, while D. G—'s shows at times a very slight paresis of the left internus and rectus superior, without double vision. Both have a slight nystagmus towards the removed hemisphere (no barbiturates), and it may be worth while to remember that both have damage to the remaining frontal lobes. D. G— does not show any pyramidal signs on the right (healthy) side, while V. R— at times has some slight spasticity in the left (" healthy ") leg, with usually some of the spastic small toe reflexes being present. The skin temperature of V. R— is, unless it is very cold, practically the same on right and left, while D. G—'s hemiplegic limbs are somewhat colder than V. R—'s, but much less so than those of the other three patients.

II. *The " Diffuse Group."* (I.Q. much lower than of the first group.)

Their hemiplegias are comparatively worse than those of the first group, and particularly that of A. L— which resembles that of a grown-up person. The reason for this, in the latter patient, is obviously due to the fact that, prior to operation he had some extrapyramidal, but practically no pyramidal disturbance. This means, he obtained a pyramidal lesion, not when he was an infant, but when he was 12 years old (by operation). J. M—'s hemiplegia of the arms was fairly severe too and is still ; possibly due to the fact that both hemispheres are involved ; he had, and still has, pyramidal signs on right and left. A. L— and A. Z— have no contracture of the upper limb, J. M— has. A. L—, who is on barbiturates, has a slight nystagmus, J. M. also on barbiturates has not ; otherwise the eye-movements of all of them are free.

B. *Sensory Functions.*

In this respect I shall deal only with the first group (the I.Q. of the second group is much too low to make an exact examination possible) and want to make two points on " epicritic " sensation : (1) V. R—'s sensation is so good on the hemiplegic side, even on his hands, that he will rightly recognize direction of movements, and also touch with cotton wool, no matter whether the right or the left, or both sides together are touched. He also can often, though not always, differentiate whether an object is hard or soft, smooth or rough. However, two-point discrimination on the right hand is less good than on the left, particularly in the region of thumb and little finger, and the same holds good for very fine joint movements. But for practical purposes his epicritic sensation is unusually little damaged.

(2) The other point is of sensory training: before a very accurate examination of sensation had been carried out on V. R—, it was found that stereognosis with the hemiplegic hand was bad. Since then (during the last three weeks or so), a charge nurse at Harperbury has, on my suggestion, tried to train V. R—'s stereognosis, with the result that he will now usually recognize: key, fountain-pen, wooden brick, comb and a penny. However, he tires very easily in this, and once he has made one or two mistakes, he relies on guessing. This is a phenomenon quite well known to occur when there is cortical defect. As a "negative complement" to this, D. G—, in the beginning, due to frequent testing, was able to differentiate the direction of finger movements of the hemiplegic hand and to imitate then correctly with the other, unless the movement became very small. Then he relapsed and refused for two years to undergo treatment until about one month ago. His joint sense is now very bad indeed. It appears to me that the retraining of finer functions has to be rigorously maintained (i.e., that it has to be practised every day, of course, without fatiguing the patient), otherwise the newly "learned" function is very quickly "forgotten." I have had similar experiences with regard to the learning and "forgetting" of finer controlled finger-movements (V. R— and A. Z—). Altogether the training of these patients, except V. R—, demands a good deal of patience, consequent to their low I.Q., lack of attention and concentration, easy fatigue and very unbalanced personalities (particularly A. Z— and D. G—).

c. With regard to *mental improvement* the best success was with A. L—, who, soon after operation, became a very happy, sociable and affectionate, though somewhat noisy child, despite maintenance, and for a time even worsening of epilepsy, and the acquisition of a severe hemiplegia. In contrast, A. Z—, another "diffuse" patient, began only recently to settle down at Harperbury Hospital, while at Shenley he is still giving a good deal of trouble though gradually less than before. In contrast to A. L—, this boy has remained free from epilepsy. So this factor in these two patients does not play any rôle concerning "mental improvement." On the other hand, the co-influence of personality factors and psychogenic conditions cannot always be excluded. A. Z— is and was a difficult child with a, until recently, not very co-operative mother, while A. L—'s parents are very devoted to him. Similarly, V. R—, who still has epileptic "equivalents," about two or three per month, has definitely improved in spite of this. But there may be some "external" factors as well at work influencing his behaviour. On the other hand, D. G—, although free from epilepsy for the last year, is still extremely difficult indeed, and I am not sure that the present "improvement" will last. One may say that the reason for the lack of success in this case, as in that of J. M—, lies in the fact that both patients have their remaining hemispheres damaged. But then V. R— (also "cystic") has frontal brain damage "similar" to that of D. G—, plus a slight disturbance of the "better" pyramidal system. So these few patients show that the position is far from being clear, when and when not to expect mental improvement from hemispherectomy, unless the patients are "picked" with the greatest care.

Having emphasized some of the difficulties which confront us with the selection of the individual patient and the evaluation of the different factors before and after operation, I want now to deal with some problems from a more general point of view.

III. Discussion. Facts and Hypotheses.

In this paper I shall deal with the more anatomo-physiological aspects of the following problems ; more shortly and at the end, the selection of operation and of patients ; more extensively with :

Hemispherectomy (H.E.), particularly in infantile hemiplegia, and in connection with the problem of production of symptoms and the possible replacement of function after interference by either a pathological process or the neurosurgeon's knife, causing elimination of that tissue which is usually thought to carry out the function concerned. By replacement of function I do not mean restitution of function which is due to the healing of a pathological process with restoration of the tissue to more or less its original state. I also wish you to understand that in this paper I speak of replacement of function essentially from the " practical point of view " ; neglecting e.g., that with a hemiplegia the chronaxy of the clinically unaffected side is altered, or that after right hemispherectomy (H.E.) in adults, according to Rowe (1937, 1938) and also Bell and Karnosh (1949), a slight lowering of emotional control and of memory function can be found when appropriate psychological tests are applied. I shall also neglect some transient disturbances after H.E. in infantile hemiplegics and adults operated on for brain tumours, such as profound loss of sensation (Krynauw, 1950*b*) or severe flaccid paresis of the hemiplegic side, or tremulousness of limbs, etc. (Cairns, 1951). On these transient findings not only nervous organization but operational factors may have an influence (Graham Brown, 1927).

Production of symptoms, according to Hughlings Jackson, is due to loss of function (negative signs) with or without the release of lower functions (positive signs). In principle, central nervous functions after loss of tissue can be replaced or maintained only when there are other parts of the C.N.S. anatomo-physiologically capable of carrying out such functions, spontaneously or after training. The classical neurological view has led us to believe that, "in man" at least, damage to function-bearing tissue may result in restitution but not in replacement of function. The most astonishing outcome of right H.E. in brain-tumour patients (later on referred to as " adults ") is that, except for the loss of function, due to loss of essentially unilaterally innervated projection areas, the disturbance of other functions is negligible ; even the hemiplegia and loss of sensation in most cases are less severe than expected. In hemispherectomized infantile hemiplegias the only total neurological loss is, as in adults, homonymous hemianopia, with or without macular sparing. There is usually improvement of motor function, mainly due to training (case A. L— is an exception). Sensory loss is often amazingly slight, and retraining appears possible (D. G—, V. R—). More than this : removal of the so-called dominant hemisphere does not produce apraxia for objects, nor aphasia and kindred disturbances (all cases). On the contrary, speech may improve after operation (cases A. L—, V. R—, A. Z—, some of Krynauw's patients). Other loss of functions met with after "pathological" damage to association areas of the subdominant hemisphere will also not occur. This appears to prove true what has been assumed for a long time, as patients with early right infantile hemiplegia usually can speak well (some French writers are of a different opinion, e.g., Klein, 1949), that the very immature brain, possibly with undeveloped myelinization, is very "plastic" and that the better hemisphere can take on the association-functions of both hemispheres, becoming dominant and subdominant at the same time. The "plasticity" of the immature brain extends to a certain degree even to *projection* functions. The loss of motor and sensory functions in infantile hemiplegias is often less severe than in patients who received their lesions at a later time in corresponding areas. Most likely, in such early cases, the ipsilateral and subcortical systems are able to develop (spontaneously and/or by training) some of their functions to a higher degree. An exception to this is the visual field, with the possible exclusion of the innervation of the macula; crossing (or uncrossing) of fibres appears to be practically complete. Our patient A. L— proves the hypothesis that the brain has to be very immature in order to develop homolateral and/or subcortical motor and sensory functions after a lesion. A. L— was only 12 years of age when hemispherectomized. While before operation the motor disability was essentially extrapyramidal, he is now left with a very severe hemiplegia indeed.

It would be very superficial, however, to assume that "plasticity of the immature brain" gives the whole solution of the problem of production and replacement of function after cortical lesions.

(1) Even in adults subdominant H.E. does not produce either the disturbances we connect clinically with damage to the temporal and parietal areas, or the so-called homolateral frontal syndrome of the French authors ("extrapyramidal" disturbances and dis-coordination, Rouquier, 1948), and above all:

(2) If the plasticity of the immature brain could overcome everything, why is there infantile hemiplegia with mental and epileptic phenomena at all? Krynauw thought, and this was the rationale for his operation, the syndrome is not so much caused by loss of tissue as such, but by a pathological process whose upsetting influence spreads not only to many areas of the diseased hemisphere, but also through the corpus callosum and other commissural systems to the other hemisphere. Removal of the disturbed and disturbing hemisphere should allow the cortex of the other one to carry out and develop its functions, and we may add also the functions of the bilateral deeper parts of the brain. On the other hand, a number of functions in infantile hemiplegics remain damaged or become lost even after surgical intervention, so another factor apart from "disturbance by a pathological process" must exist.

We must therefore restate our problem of disturbance and replacement of functions consequent on surgical or pathological interference and ask: what kind of damage in what areas does, or does not, cause production of symptoms? You will remember from the way patients were presented that the crucial point appears to be whether damage is produced in "projection" or in "association" areas, and whether the functions, physical or not physical, are "innervated" or "localized" or "centrally" organized, or "represented" if you prefer the Jacksonian term, essentially uni- or bilaterally in the cerebral cortex. I speak again from the practical point of view, because "theoretically" representation of function is distributed all over the brain, but "practically" concentrated in preferential parts, the so-called "centres." Functions are evoked by peripheral or central stimuli travelling along afferent pathways. They are then integrated in or by central systems, usually in and/or around (synapsis) cells, and their action, again central or peripheral, is carried out by effector systems through the integrated stimuli travelling along efferent pathways. The more complicated a function is, the more complicated is the nervous organization serving it and vice versa.*

Hughlings Jackson has taught us that functions are built up at different levels, subcortical and cortical. In the evolution and dissolution of functions many factors play a rôle. This is all somewhat complicated, but over-simplification of a problem obscures it.

Now let us turn our attention to the difference between pathological and surgical lesions. A pathological process, and particularly a diffuse one, may cause quite irregular lesions, unselectedly affecting one or several systems, or parts of them, to a varying degree, extensively and intensively. Such a lesion may not simply produce elimination of a system and loss of function, but from it inadequate and faulty innervation with distortion of function may result, the more so, the more systems are affected and the more complicated a system is: i.e., particularly in association systems. To this, the possible localization of a process, are added the many mechanical, chemical, physiological, vascular, direct and indirect, local and remote consequences of a lesion. Wertham and Wertham (1934) list about 35 different aspects of a demyelinating lesion. Thus, the consequences of pathological processes may spread far beyond their actual "anatomical localization" and influence ipsi- and contra-lateral hemispheric functions, and due to the interference with the association and commissural cells and fibres, the lesion and its consequences may disturb just those systems with which the damaged areas are most closely connected and which otherwise might be able to replace or maintain the functions locally disturbed or cut out. A pathological process is often something very much alive (and developing over many years after the original damage). Krynauw's and other neurosurgeons' ideas of spread of disturbance, not only of epileptic discharges, appear to be supported by the fact that the E.E.G. of the healthier side, usually abnormal before operation, as you remember from the Q.S. reports, becomes more normal afterwards. Krynauw (1950), Obrador and Laramendi (1950) and some electroencephalographists hold the view that the pathological spread is of a physiological, and not of an entirely physical nature. This point is, however, still under discussion. Anyway, from the practical point of view, Krynauw's contention appears to explain both :

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* The central organization of such areas is modified by the ratio of crossing/non-crossing pathways, and the quantitative organization of handedness (right, left, mixed) may be influenced by this ratio as well (Glees, 1952). This could partly account for differences found in the individual patients. Cortical organization "itself," quantitative and qualitative, will also play a rôle: "projection" areas e. g., do not only consist of the cells and layers which recieve or emit "projection" fibres (and the functions connected with them, e.g., "motor" or "sensory"), but also many others. One wonders whether, for instance, the differences in skin temperature in our different patients may be connected with vegetative homo- and bilateral representations in essentially motor or sensory "centres," because, as far as we could make out, the severity of the hemiplegia itself does not account for individual differences.

> (1) The reason why even a plastic immature brain is unable to cope with the influences of the pathological process and its consequences, and (2) why hemispherectomy relieves many symptoms. Surgical intervention will do away with the pathological damage, and although elimination of entire physiological systems may lead to loss of functions and possibly release of some positive signs, the creation, at least in many cases, of a clean symptomless scar, will bring to an end interference with ipsi- and contrahemispheric systems, and systems which can potentially replace or maintain functions are now enabled to do so.

With regard to transcallosal spread I am, however, touching a very dark field. We know from clinical and physiological facts that electrical and pathological stimuli can spread contrahemispherically, and clinical disturbances result from pathological lesions. On the other hand, a clean total surgical section of the corpus callosum and even at the same time, of one fornix does not lead to any appreciable disturbance of any function, not even to apraxia, or certain agnosias, unless such functions were damaged before section. People can learn new bimanual activities after section of the corpus callosum and one fornix. (Akelaitis *et al.*, 1941, 1942). One wonders what the normal functions of the corpus callosum is ; although the results reported confirm in principle the different effects of surgical and pathological lesions.

Let us return to our subject : symptom-formation and replacement of functions, and let us discuss shortly the question of loss and replacement of function with regard to the main cortical projection and association systems. Anatomically and electrophysiologically this division does not hold entirely good any more. From our present clinical knowledge and for practical purposes it still appears that the main function of projection systems is reception or emission of simple or integrated stimuli. Destruction of " centres " appears to be equivalent with the interruption of the function-carrying axons. This may lead to abolition or weakening of function, to release of " positive signs, " possibly also to some irregularities, but as the *function-carrying axons* come up from, or go down to the periphery and do scarcely cross through commissural systems to the other hemisphere, " interference " with function, if any, will be slight, even when there is bilateral representation.

The activity of association systems, on the other hand, is of a more complicated nature. They do not deal any more with originally physical stimuli, but with complicated nervous processes built up from them at a much higher level ; or by " differentiating " such high level functions they lead to physical actions. Many of the function-carrying axons of these systems lead to other association-areas on the same or the other hemisphere. Consequently, disturbance, inadequate and distorted innervation is apt to spread homo- and heterohemispherically, and replacement or maintenance of functions by corresponding systems will become difficult or impossible, as these systems are now disturbed. This is one *possible* explanation of the phenomena which I am going to describe now, whether it is the *right one* I am not quite sure.

A. *Projection Systems.*

I. *With Essentially Unilateral Innervation.*

Loss of tissue as well as interference causes loss of function. Pathological processes may lead to epileptic discharge. There is little replacement, particularly of the highest functions. In principle: the more highly specialized, and more peripherally "lateralized" a function is, the less there is ipsilateral representation through uncrossed pathways (? unless there is anatomical ambidexterity). Any postnatal development of ipsilateral cortical functions after damage to the main contralateral system appears to be dependent on the age of the brain at the time of lesion and the massiveness of the lesion. Compare cases D. G— and V. R— with cystic disturbances and fairly good peripheral movements with the other diffuse cases which are worse. Remember again case A. L— with the severe post-operative hemiplegia caused by cutting of an originally functioning pyramidal-system which had not forced or enabled the ipsilateral hemisphere to develop these functions at an early age. The high achievement of epicritic sensation in fortunate cases (possibly ? ambidexterous) is also very interesting. V.R— learns now stereognosis. Also, D. G— had acquired some sense of joint feeling and lost it after not training for two years. with regard to motor function there are some cases in the literature which after more or less intensive training could carry out isolated finger movements (Foerster, 1936). The question arises which rôle subcortical systems may play, and it seems wise to me to preserve the caudate nucleus.* The reasons, apart from those given already, why pathological interference with function does not lead to spread may be:

(1) *Motor systems:* The arm and leg area of the so-called pyramidal system according to physiological experiments by Bailey, McCulloch and Garol (1941) have only few, if any, trans-callosal connections.

(2) *Sensory systems:* Multiple innervation is better developed. Although trans-callosal connections are plentiful they are most likely not of "function-carrying" nature, and also the sensory cortex like the motor most likely too, may be able to suppress to some extent disturbing stimuli. Apart from this, thalamic activity, possibly even for touch, may help to maintain normal function and to repress interference. A third reason for the minimum of spread may be as I have already said, the comparative simplicity of function in only one direction (peripherally) of afferent and efferent projection systems.

II. *With Essentially Bilateral Innervation.*

Replacement or maintenance of function after unilateral central disruption is good, due to bilateral innervation, unless the damage is very large (tumours, cysts with changing fluid content, etc.), and causes by mechanical pressure, or collateral oedema, or vascular processes, etc., the other hemisphere to become involved.

There are plentiful trans-callosal anatomo-physiological connections, but spread of pathological interference will be small for the reasons already given.

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* As Krynauw demands.

To this may be added that adequate and appropriate innervation (afferent and efferent) possibly helps to suppress interference and faulty and inadequate innervation. Yet another factor may be the obscure nature of the commissural systems, generally, and with regard to different functions in particular. You may remember what I told you about the corpus callosum. Possibly there is, however, another entirely different explanation, as I shall show later: namely, that the role of anatomo-physiological spread is exaggerated altogether.

B. *Association Systems.*

These I have subdivided into those with essentially unilateral innervation and more absolute or relative dominance, and those with essentially bilateral innervation: co-dominance. This classification with a view to mixed-handedness and a good deal of clinical ignorance or obscurity has to be taken with quite a large grain of salt.

I. *Absolutely dominant* are those centrally represented functions, intimately connected with the motor, sensory and gnostic use and skill of the dominant hand and their respective projection systems; functions such as speech, possibly some forms of object-praxia and the more symbolic functions arising from them. Loss of function takes place after surgical and pathological interference. Replacement is better in immature than in adult persons. Due to their nature as association-systems, faulty and inadequate innervation and consequent dysfunction is frequent after pathological lesion. There may be spread to and interference with the possible compensatory functions of the subordinate systems, but apparently not, or not markedly so, the other way round, except in mixed handedness, although in these and other persons, retraining of the functions damaged and making the subordinate hand dominant, has often a beneficial effect. ("Shift of dominance," Nielsen, 1946, Orton 1937).

II. *Relatively dominant* are systems more or less intimately connected with the functions of the subdominant hand (Fleischhacker, 1947) and side of the body, and those afferent and efferent innervations of non-autonomous and autonomous nature, arising from both sides of the body, which build up the motor and sensory functions of what we call the image of the body, possibly also identification of persons (in this last respect I (1947) disagree with Nielsen (1946). When these systems become disturbed through pathological processes, in adults as well as children (on the right posterior half of the brain in right-handers), apraxia for dressing and disturbance of the body image is often the result. Possibly, the left hemisphere is relatively subdominant for some forms of eupraxia. However, after hemispherectomy, these functions are practically replaced by the relatively subdominant hemisphere, after a shorter or longer interval, in infantile hemiplegias and adults. Why pathological disturbances in the relatively *sub*dominant areas despite the many trans-commissural connections do "practically" not interfere with the functions of the relatively dominant ones, I find difficult to explain. Possibly, the "relatively dominant" systems are quantitatively more developed and provide therefore adequate innervation with the power to suppress disturbances from the other hemisphere, which the subdominant have not ; or it may be that, at least with regard to the body image only the relatively dominant hemisphere (but not the subdominant one) contains " subjective " systems whose damage leads to disturbance of this function.

III. *Co-dominant functions* are essentially bilaterally represented. They appear to be very little dependent on the functions of a preferential limb or side of the body. Stimuli arise from "without," from all sides of space, essentially through eyes and ears, and from the organism itself, posturally, vegetatively, instinctually, etc. The functions concerned are, from our present knowledge, those of orientation in space and place, and those of a more "personal" or subjective nature, as character, temperament, mood, etc. However, even here we find a certain lateral dominance. Disturbance of will and mood and their influence on intelligence are more "localized" in the left frontal brain (Petrie, 1952). Restlessness, resistiveness are encountered more often when the right frontal brain (Fleischhacker, 1951) and impulsiveness and irritability when the right temporal lobe are more diffusely damaged. There is apparently close collaboration between the two hemispheres of the brain, and with pathological lesions interfering spread from one hemisphere to the other, particularly after damage to systems concerned with more "subjective" functions, occurs in immature and mature persons. On the other hand, surgical elimination of tissue will allow considerable replacement or maintenance of function (all infantile and adult cases, taking into account *the mental deficiency* of the former).

There is, however, another entirely different explanation of disturbances arising from pathological processes in co-dominant and possibly relatively dominant systems, which does not necessitate the assumption of anatomo-physiological spread through the commissural systems. Orientation, for example, is dependent on the way bilateral stimuli come in and are co-ordinated and fused. Now, if one hemisphere receives adequate and the other inadequate and distorted stimuli, this co-operation or fusion will not take place in an orderly fashion and confusion must arise. Indeed, Sherrington (1948) has shown that for the fusion of optic patterns in corresponding visual fields trans-callosal anatomical connections are not necessary, as long as the stimuli arrive adequately in time and place in corresponding parts of the retinae and calcarine areas (see also corpus callusom, p. 79).

This is what I had to say on some factors influencing the production of cortical symptoms and replacement of function after surgical or pathological lesions. Now I want to talk shortly on two other problems : the selection of operation and the selection of patients for operation. Krynauw, now supported by Carmichael (1953), thinks that infantile hemiplegia with character disturbance and epilepsy should always be treated by total hemispherectomy, irrespective of loss of some projection functions ; their argument is that there are patients who have become worse after partial-ectomy, and then improved when the rest of the hemisphere was removed. On the other hand, some French authors (Klein, 1949, and also Henyer, Feld and Hourmak, 1951), and also Wilder Penfield (1952) are of the opinion that removal of the pathological tissue is sufficient and the rest of the hemisphere left (after creation of a clean surgical scar) will persist to function. The two main problems involved are apparently :

> (1) Does one hemisphere, from the practical point of view, function as a whole ? or, to put it differently, does a hemisphere of which large parts have been eliminated, become so disturbed that it will disturb the other to a high degree as well ? This is not necessarily the case, possibly except for a period of temporary diaschisis, as we know from lobectomies. We know also that aphasia does not necessarily involve reading, writing, and eupraxia to a *great* extent, etc. On the other hand, we know from the investigations of Rowe (1937, 1938), and also Bell and Karnosh (1949) that total-ectomy of the so-called subordinate hemisphere *in adults* causes some character disturbances. From the physiological point of view, I would think that partial-ectomy is no contra-indication as long as systems are excised or interrupted in such a way that there is a minmium of faulty or inadequate innervation with all its consequences.
> (2) Is it always possible to remove all damaged tissue ? This depends mainly on the nature of the process and the possibility of diagnosing this and its extension. In essentially diffuse (or dispersed) processes total hemispherectomy appears to be the best solution (cases A. L—, A. Z—). In more circumscribed processes (cysts and large solid scars) which have left the remainder of the tissue intact, a more local operation should suffice. But on this point there is no agreement, and we shall have to wait until greater knowledge is available.

I come now to my last subject : the selection of patients for the operation. One may ask the question : selection from which point of view : improvement or cure of epilepsy, or of personality disturbance, or both ? In this respect we know very little. As pointed out in the beginning, A. Z— (diffuse process) and D. G— (cyst), have now been free from epilepsy since operation or for a year respectively (D. G— despite frontal brain damage), but A. Z—'s behaviour is only somewhat, D. G—'s scarcely better.* On the other hand V. R— (cyst), is still having occasional epileptic episodes, but despite this and damage to the remaining frontal pole and the "healthy" pyramidal system, he has mentally improved (some psychological factors may be involved), and A. L— (diffuse process), despite a temporary increase of epilepsy, and the occurrence of severe hemiplegia after operation became nearly at once an entirely changed person, and from the mental point of view he is the best of our group. From these contradictions it appears that much has to be learnt.

If one wants to be sure of total success, the postulates of Krynauw and Cairns (1951) that only one hemisphere is involved, the personality good and the grade of mental deficiency not too low, should be fulfilled. Possibly one might add that institutionalization should not have lasted too long, or better still, the process should still be active and threatening institutionalization. In younger patients, collaboration of parents should be good. A. Z— is very much influenced by environmental conditions (parental attitude, etc.). Much

* J. M— was known before operation to have both hemispheres involved, a very low grade M.D., rather severe hemiplegia and pyramidal signs on both sides.

more has to be known on the different causes of personality disorders. Developmental retardation or standstill, violence, temper tantrums and other kinds of lack of control, restlessness, moodiness, etc., may be due to quite different causes or combinations of these :

(1) They may be reactions of an easily frightened, depressed, but not necessarily unbalanced or bad personality, to the illness with all its consequences, including medication ;

(2) they may be the outcome of a very unbalanced personality, either originally so by constitution, or due to strong adverse psychoreactive situations later ;

(3) they may be the consequence of the disease proper, either affecting the whole brain or parts of it, uni- or bilaterally, cortically or subcortically, more focally or more diffusely, and, if unilaterally, with the possibilities of disturbing contralateral systems.

When I discussed association areas, several "localizing characteristics" of diverse personality disturbances were mentioned. Clinical psychiatry and psychology should try to achieve a better understanding of these problems, in order to give us guidance in this matter.

I wish to thank Dr. E. Taylar, Medical Superintendent, Harperbury Hospital, for having given me the opportunity to study these five patients.

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INTENSE ULTRASOUND—A NEW TOOL FOR NEUROLOGICAL RESEARCH.*

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A FOCUSED beam of ultrasound can be used to produce selective accurately localized lesions in central nervous systems which are quantitatively reproducible from one animal to another.

Discrete lesions can be produced without destruction of blood vessels. The extent of the destruction can be limited to nerve cell bodies only, nerve fibres traversing the irradiated region are left intact and functioning. By careful control of the dosage it is possible to effect a differential destruction of large nerve cells leaving the population of the small nerve cells in the same region essentially unchanged.

The lesion can be accurately localized by focusing a fine beam in the region to be affected. Beam widths of two or three millimetres are readily attained. We have used both a single beam focusing irradiator, which produces a lesion small in cross section but relatively long and a multiple beam instrument which is suitable for producing lesions small in all three dimensions.

The nature of the destruction depends on the intensity and duration of the exposure. Dosage studies made on a series of animals can be used as an accurate guide in choosing the conditions of irradiation for structural and functional studies.

The bibliography at the end of this paper can be consulted for detailed articles concerned with the subject matter of this paper (1–7).

We will illustrate the differential selectivity possible for affecting large cells only, by some results of a study currently in progress on the motor cortex of the monkey, *Macaca mulatta*. The conditions for irradiation and the results obtained in one experiment follow. The sound level and duration were chosen so that the large cells of the cortex would be destroyed but the smaller cells would be relatively unaffected. The sound was focused in a pattern of overlapping spots the majority being located in the hand and arm region of area 4 of the right cortex. The duration of the exposure was 4·0 seconds and the intensity was 70 watts/cm^2.

The animal was sacrificed one month after exposure. Histological examination showed that the majority of the Betz cells in the exposed area were destroyed while the smaller cells were relatively unaffected. Fig. 1 and 2 illustrate this differential destruction. Fig. 1 shows a section of the left motor

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cortex which was unirradiated. One notes the presence of the large Betz cells in this normal cortex. Fig. 2 shows the corresponding portion of the right motor cortex which was irradiated. The population of Betz cells in this irradiated cortex is greatly reduced while the population of the smaller cells is practically unaffected.

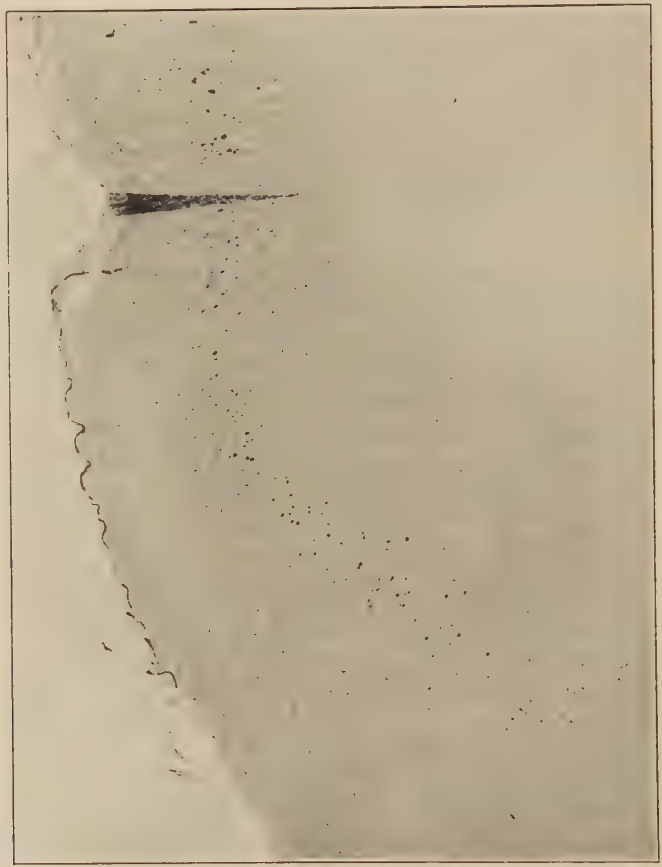

FIG. 1.—A section through the motor cortex (left) of *Macaca mulatta.*

Marchi studies of the spinal cord demonstrate degenerating fibres in the pyramidal tract but not in the ventro-medial tract. Fig. 3 shows Marchi preparations from three levels of the spinal cord. The upper section is taken from the cervical region, the middle from the thoracic, and the lower section from the lumbar region.

Studies currently in progress have as their objective the determination of possible functional and cortical electrical excitability changes in animals with such motor cortices. With this tool it thus appears possible to check by direct means the importance of the large pyramidal cells by removing them and leaving the remaining components of the tissue intact.

It should be noted here that the primary action of the sound is not the total disruption of the nerve cell body. No change is observed histologically in nerve cells fixed immediately after irradiation and stained with toluidine blue. This is in contrast to functional or electrical changes which are apparent immediately after irradiation. For example, the paralysis of the hind legs of a frog following the irradiation of the unanaesthetized animal over the region of the lumbar enlargement is evident immediately after the irradiation. Lighter doses do not cause a delayed paralysis.

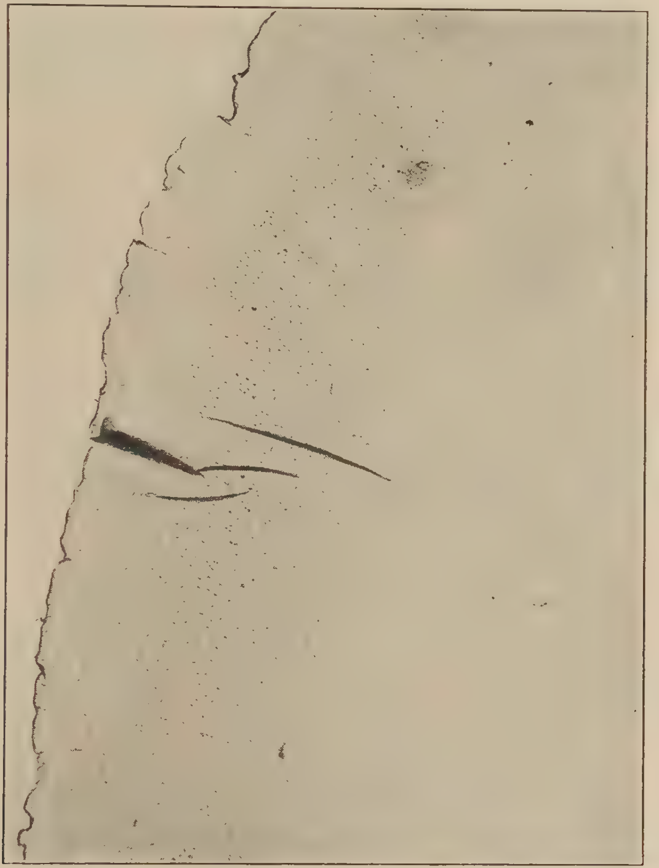

FIG. 2.—A section of ultrasonically irradiated right motor cortex from the animal of Fig. 1. This section corresponds to that of Fig. 1.

We can illustrate the possibilities of this technique for affecting deep structures by the results obtained in a study of the bulboreticular inhibitor formation of the cat. The sound passed through the cerebellum and the fourth ventricle before reaching the bulboreticular formation. A series of separate irradiations was carried out so that the focal point moved over the whole area in which the large cells of the bulboreticular formation lie. This region is so close to respiratory and other vital centres that almost all previous attempts to produce lesions in this area by electrolytic fulguration have resulted in the death of the animal due to swelling of the brain stem and interference with the blood supply.

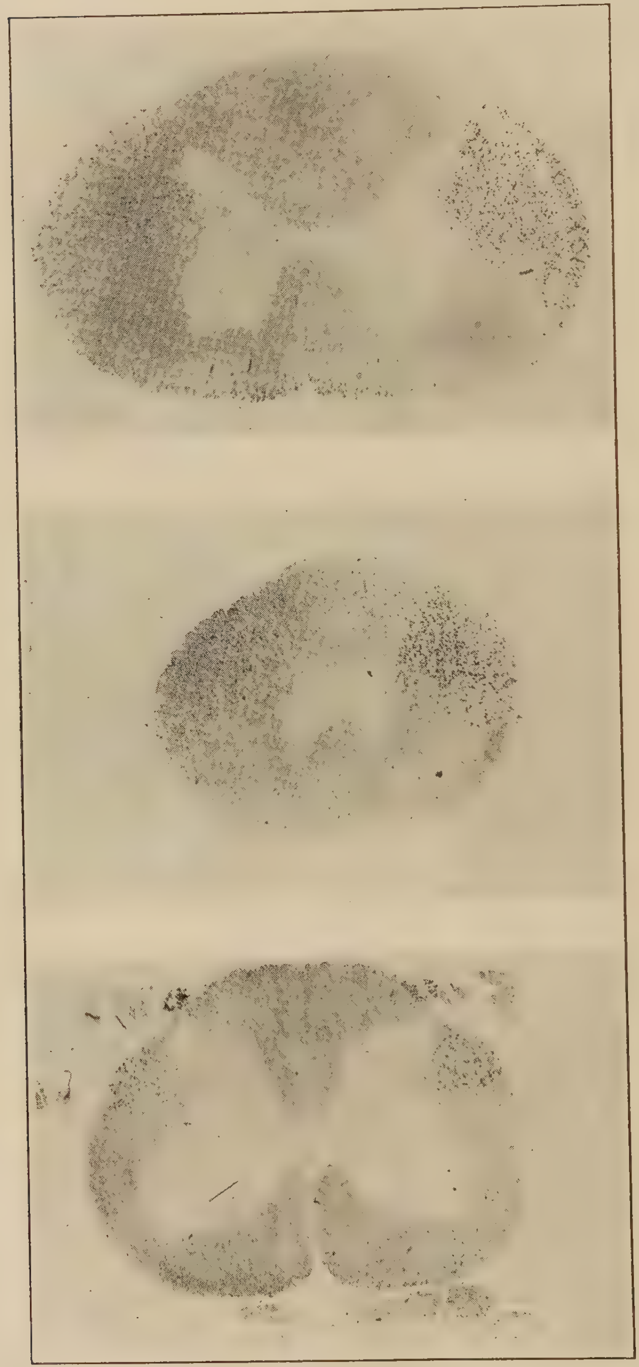

FIG. 3.—Marchi preparations from three levels in the spinal cord of the animal of Fig. 1 and 2.

None of the animals irradiated showed signs of respiratory disturbance or vascular collapse after the irradiation. The animals recovered rapidly and showed a striking and permanent abnormality of the motor system. The resting posture was with hyperextended fore limbs and slightly flexed hind limbs. On walking the fore limbs showed a goose step and the hind limbs a wide base with circumduction. The fore limbs showed an exaggerated grasp reflex. In one animal followed over a period of two years no changes of this motor deficit have been seen.

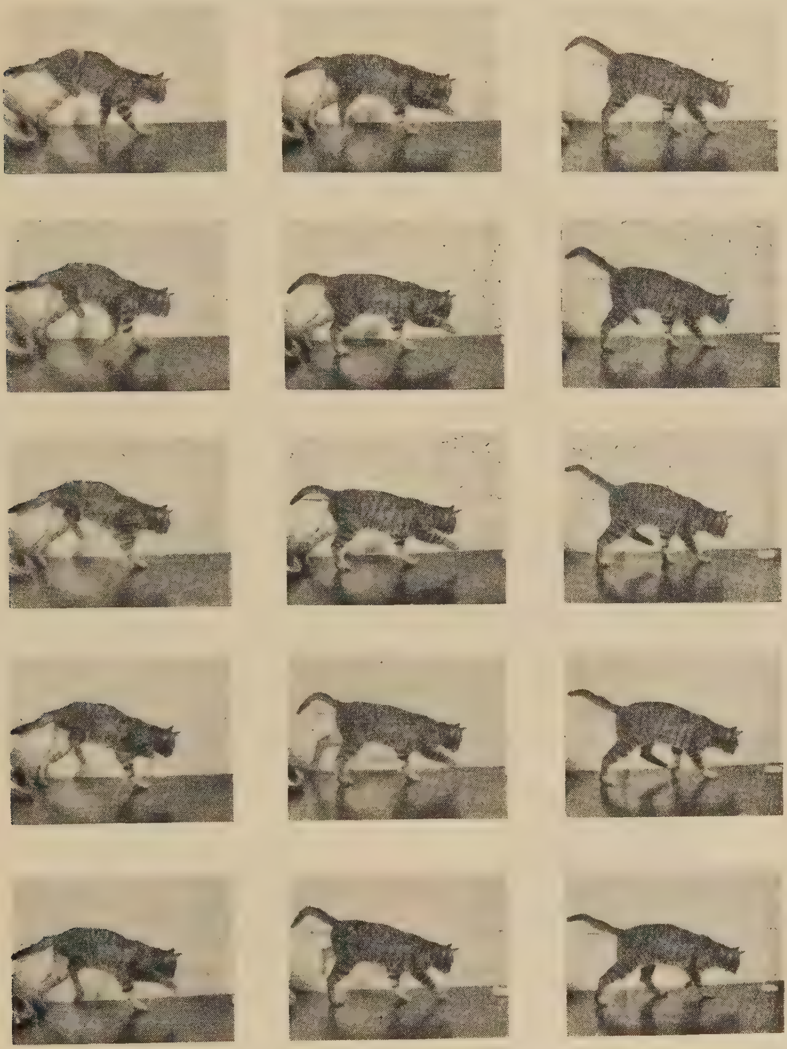

FIG. 4.—Typical walk of a cat with an ultrasonicallv produced lesion in the bulboreticular inhibitory formation.

Histological examination of the bulboreticular formation showed a depopulation of cells. The beam produced a lesion whose lateral borders were sharply localized but, because of the long focal length, had the effect of irradiating cells for some distance above and below the region with sound above the threshold dosage. Consequently, the cells in the roof nuclei of the cerebellum were also damaged.

Further studies of the bulboreticular formation will be carried out with a multiple beam instrument in order to eliminate any damage to nearby cells in the cerebellum.

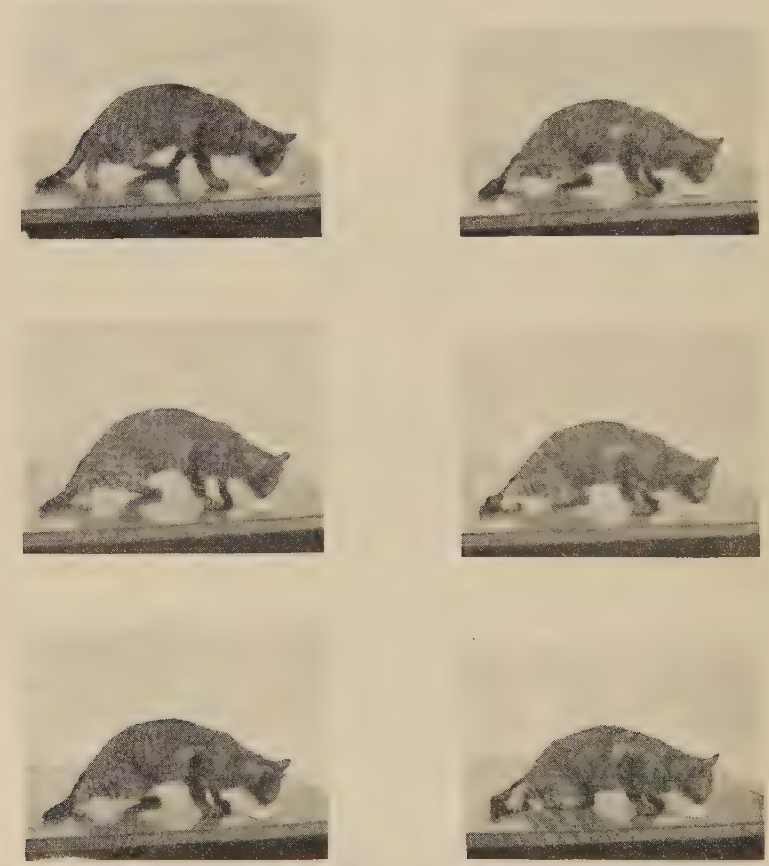

Fig. 5.—Awkward positioning of hind limbs in a cat with a lesion in the bulboreticular inhibitory formation produced by ultrasound.

Fig. 4 and 5 are illustrations of a cat with an ultrasonically produced lesion in the bulboreticular inhibitory formation. The pictures were taken approximately 5 months after irradiation. Fig. 4 shows the animal walking. The goose stepping is readily seen. In Fig. 5 the animal is shown drinking milk from a shallow dish. Awkward positioning of the hind limbs is illustrated in this figure.

Most of our work up to the present time has been accomplished at a sound frequency of 1·0 mc. using a single beam focusing irradiator. The sound is generated by a vibrating quartz crystal and focused by a lens. Transmission of the sound from the irradiator to the tissue is accomplished through physiological saline. This liquid must be degassed to prevent the formation of bubbles, which would interfere with the transmission of the acoustic energy. The bone overlying the region of the nerve tissue at which the sound is to enter the central nervous system must be removed in order to prevent overheating and to insure a well defined focused beam in the tissue.

The single beam type focusing irradiator produces a pencil-shaped lesion, that is, one which is small in cross-section but relatively long. This type of lesion is not suitable for many neuroanatomical or neurophysiological studies. Consequently a multi-beam instrument has been developed and work has been started with this apparatus. The device consists essentially of four single beam focusing irradiators coupled together mechanically with a suitable number of adjustments to enable the beams to be brought into coincidence. Much smaller lesions can be produced with this multibeam arrangement than can be attained with the single beam apparatus.

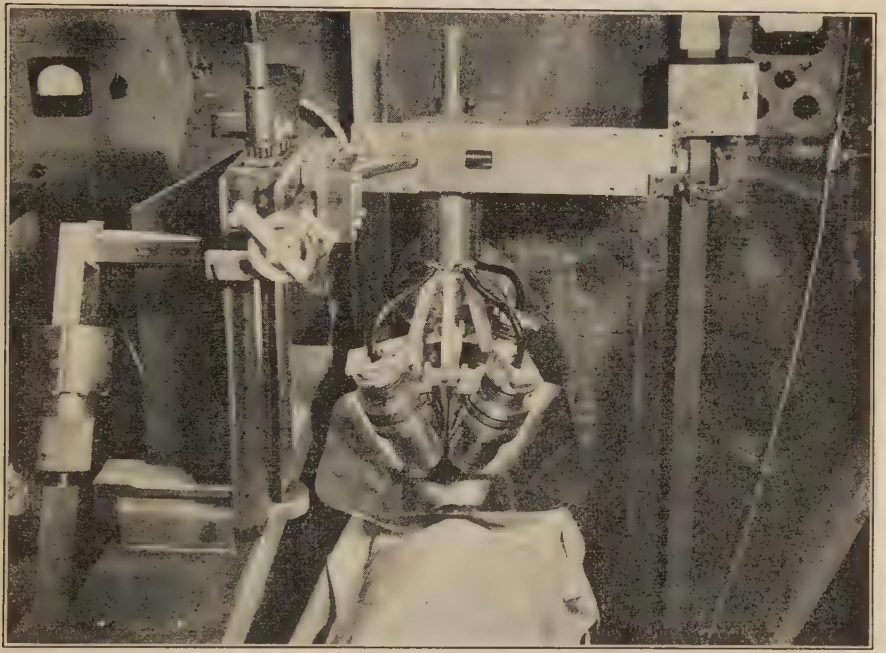

FIG. 6.—Multibeam irradiator and partial view of experimental arrangement for producing lesions by ultrasound in the central nervous system.

Fig. 6 illustrates the multibeam instrument and a portion of the experimental arrangement for carrying out the irradiation. In practice the animal is supported in a standard Horsley-Clark apparatus partially visible in Fig. 7. The flanged cap, used to support the physiological saline, which acts as the transmitting medium for the sound, is tied to the skin of the animal. Fig. 8 shows a close-up view of the multibeam instrument positioned over the head of the animal. The cortex is exposed for irradiation. It is not necessary to open the dura unless a visual study of the cortex configuration is desired.

A study of the physical factors involved in the production of the physiological changes is important from the viewpoint of the fundamental mechanism of the action of the sound on the tissue. We will now indicate briefly the present status of our knowledge regarding these factors. The first factor which received consideration was temperature.

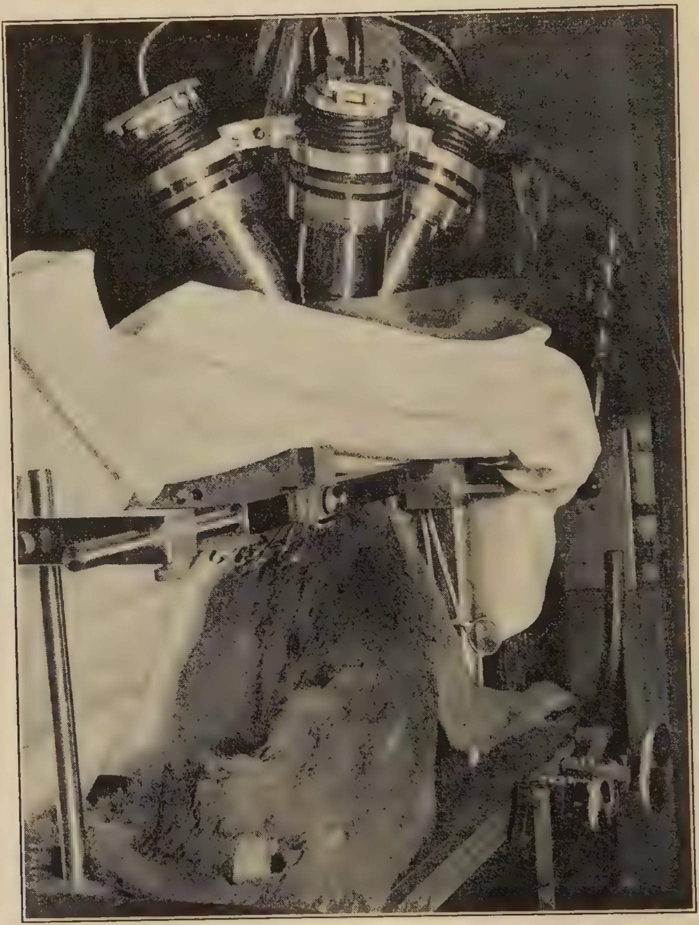

Fig. 7.—View of monkey supported in Horsley-Clark apparatus with multibeam irradiator in position.

Temperature changes which occur when ultrasound is propagated through tissue may play a rôle in producing biologic effects in the following ways: (1) the temperature of the tissue exceeds some value above which damage occurs; (2) high temperatures exist at interfaces in the tissue which are not detected by a thermocouple as small as say 0·003 in. in diameter; (3) temperature changes associated with cavitation are responsible; (4) heating at gas nuclei in the tissue is important.

Consider the various mechanisms in the order just mentioned.

(1) A number of independent arguments are presented against the possi-

bility that the temperature of the tissue exceeds a critical value above which damage occurs.

(*a*) Experiments on cooled frogs show that the ultrasound produces its effects on nerve cells when the temperature level in the cord is less than 20° C.

(*b*) Summation of the biological effects in motor neurons produced by sound pulses, separated by periods of time long compared to the interval required for the tissue to return to its initial temperature proves that paralysis is not dependent on achieving any particular temperature level.

(*c*) From experimental results obtained on frogs one can conclude on the basis of the experimentally determined linear relation between reciprocal of minimum paralysis time and acoustic pressure amplitude that the absorption of a constant amount of acoustic energy by the tissue is not required to produce the effect.

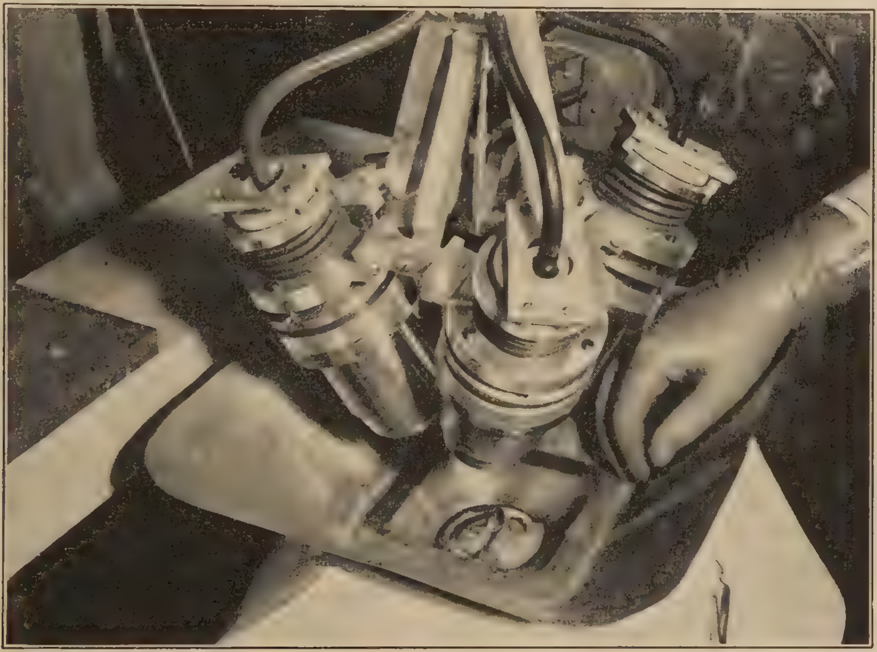

FIG. 8.—Close-up view of multibeam irradiator in position over the exposed cortex of the animal.

(*d*) Thermocoagulation studies on the cerebral cortex by McCulloch and others have shown that, when the large cells are destroyed by heating, the small cells in the tissue are also destroyed (8, 9). However, in our studies with ultrasound it is evident that the large cells are particularly sensitive to the acoustic radiation.

(2) Consider now the second possible manner in which temperature might be involved, that is through heating at interfaces. A relatively simple calculation proves that such an hypothesis is untenable. For example, we assume that all the sound which is absorbed, is absorbed at interfaces and consider a volume of material consisting of cells of diameter 10 microns. If we subject

such a material to a sound intensity as high as 100 watts/cm.^{2}, choosing as values for the physical parameters of the material those characteristic of nerve tissue we obtain for the maximum temperature rise at the interfaces a value of about 0·001° C.

(3) The third possible manner in which temperature might produce biological effects is in association with cavitation, defined here to include both the process of cavity formation and collapse in the tissue and the growth and collapse of a gas nucleus in the tissue under alternate tension and compression forces. It has been shown that the biological effects of ultrasound on the tissue of the central nervous system are the same whether the exposure is made under a hydrostatic pressure of one atmosphere or under a pressure sufficiently high to eliminate tension forces in the biological materials during acoustic propagation. This eliminates possible temperature changes associated with cavitation as important in the mechanism, since in the absence of tension forces cavitation does not take place.

(4) The possibility of high temperatures produced during an acoustic disturbance at or near the surfaces of small gas nuclei, in the absence of tension forces, must also be considered in discussing the mechanism of biological effects. A mechanism based on the existence of such temperature changes is unlikely for the following reasons.

(*a*) Gas nuclei of diameters equal to or greater than about one-half of a micron would be detectable microscopically. However, there is no evidence for the existence of such nuclei. Assume then that if gas nuclei are present they are less than one-half of a micron in diameter. Since the maximum temperature change occurs, in the imbedding material, at the surface of the bubble, and since the temperature rise increases with an increase in bubble radius we compute the temperature change at the surface of a gas nucleus with a diameter equal to one half of a micron on the basis of a formula derived by Rosenburg(10). The difference between the temperature at the surface of such a bubble and the average temperature of the medium for a sound intensity of 100 watts/cm.^{2} and a frequency of 1·0 mc. is about 0·3° C. This computation indicates that the effect under discussion cannot be important in the mechanism of the effects of ultrasound on nerve tissue described here.

(*b*) No evidence of the growth of gas nuclei is seen under the microscope in nerve tissue irradiated at a hydrostatic pressure of one atmosphere and fixed within two minutes after exposure. Vacuole formation (and probably tearing of fine fibres) would be expected if such gas nuclei exist and could grow under tension forces of the order of 15 atmospheres.

(*c*) It would be necessary to assume in addition to the existence of gas nuclei, either that the population of such gas nuclei per unit volume is greater in large nerve cell bodies than in small and is especially low in axons, or that cells of different sizes and axons contain constituents which vary tremendously in their susceptibility to damage by temperature change. Such a possibility as the latter, concerning the temperature sensitivity of cellular constituents, seems hard to reconcile with the experimental evidence referred to above on the sensitivity to heat of the cells of the cerebral cortex.

The second physical factor to receive consideration as a possible participant in the mechanism of the action of the sound on the tissue was cavitation, defined in the discussion of the temperature factor to include both the process of cavity formation and collapse and the growth and collapse of a gas nucleus in the tissue.

Since it is possible to produce by ultrasound the effects described in the central nervous system when the animal is under a hydrostatic pressure sufficiently high to prevent cavitation, then cavitation cannot enter into the mechanism. An independent argument follows from studies by Gersh and collaborators of the pathology of decompression sickness (11). These have shown that in the central nervous system necrosis is more common in the white matter than in the grey matter. This is in contrast to the action of ultrasound. The cell bodies are much more susceptible to the action of the sound than the fibres.

The physical factor now receiving consideration with respect to a possible fundamental rôle in the mechanism is viscous force action between the submicroscopical structural components of the protoplasm and the surrounding fluid. It is expected that studies as a function of frequency and in standing wave fields will elucidate this mechanism.

In conclusion we note that by accurately controlled irradiation of the tissue of the central nervous system the experimental neurologist can selectively affect the neuron population to a desired extent leaving intact the blood supply and fibre tracts in the same region, thus completely eliminating the difficulties inherent in the older methods of producing lesions. Differential destruction of the large neurons can be accomplished making possible studies of their relative importance and function. Immediate physiological change is realized along with this selectivity. Lesions of any desired shape and depth in the central nervous system can be produced without affecting the intervening tissue.

Clearly the method has considerable potential value for neurosurgery. In addition to the characteristics just mentioned, it is noted in this connection that there are no long delayed deleterious effects. Animals have been observed up to a period of approximately two years afteı irradiation with no complications appearing. It is also noted that with this method of producing lesions a rapid recovery from the operation ensues. Usually within 24 hours after irradiation the animals are active.

SUMMARY.

A focused beam of high frequency sound can be used to produce both reversible and irreversible changes in central nervous systems. The focal region of the beam can be accurately positioned at any desired location in the tissue. Intervening tissue can be left unaffected, since the conditions of irradiation can be arranged so that the sound level is above the threshold required for producing the desired change only in the focal region. The neurons are affected most readily, the vascular system and supporting structure being left intact at dosages which affect drastically the neural components. Fibre tracts are functionally unaffected at dosages which cause major changes in the operation of the nervous system, indicating that the primary action of the sound takes place at the nerve cell body or synapse or both. It is possible grossly to affect

the large nerve cells in a region and yet leave the small cell population practically unchanged.

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A TENTATIVE CLASSIFICATION OF GOAL-SEEKING BEHAVIOURS.*

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Paris.

Goal-seeking behaviour, once a great mystery, is now beginning to be understood. In its simplest forms it is, in fact, understood to-day almost completely. Thus the theory of the simple regulator, such as the thermostat, not only includes an extensive repertoire of techniques, but the elementary principles, of the necessity for negative feedback for instance, are becoming scientific commonplaces. In getting to know, however, about these simple systems and their principles, we should not make the mistake of thinking that there is nothing more to be learned. On the contrary, in real life many an important goal is to be achieved only through some quite complex pattern of behaviour, a pattern for which the simple concept of " negative feedback " is quite inadequate. It is of these more complex patterns that I wish to speak to-day.

One way of studying the subject is by way of actual experiment ; but I shall make little reference to actual experiments to-day. The fact is that before such experimentation can be undertaken with any usefulness there must be a preliminary period of study and thought. Before we can experiment we must be clear about what questions we want to ask, and why these questions are significant, and what are to be the interpretations of the experiment's various possible outcomes. Before we can usefully start experimenting, in other words, we must have a well-developed theory. Such a theory must inevitably, if it is to be precise, be mathematical ; but I hope to show in this paper that what is necessary, at least at first, is the logic and precision of mathematical thought rather than its more advanced techniques. If then we are to explore the properties of the more complex forms of goal-seeking behaviour we must first construct some suitable mathematical models.

The use of mathematical models in the study of animal and human behaviour goes back to the early nineteenth century, but those early attempts have little in common with the contemporary researches of such scientists as von Neumann, Wiener, and, here among us, Dr. Ashby. The last author has particularly stressed the similarity between the activities of some types of mechanism and that of the brain ; and this similarity must be the excuse for a mathematician such as myself venturing into this controversial field. My aim will be to show how certain of the more complex goal-seeking behaviours, seen in both machines and men, can be described, and the principles made clear, by a uniform mathematical framework of ideas.

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* A paper read at the Annual Meeting of the Royal Medico-Psychological Association held at Barnwood House, Gloucester, 9 July, 1953.

Basic Concepts.

In order to make the ideas as clear as possible I shall start with a very simple example. Let us suppose a man is on the top of a hill and that he wishes to get to a house in the valley ; let us assume that the " goal " is his arrival there in *the shortest possible time.* Between him and the house are many causes of delay : boulders, marshes, escarpments, and so on. Travelling in a bee-line is out of the question. Let us consider his possible modes of behaviour.

An exhaustive, and final, solution of the problem would be given by taking a map of the district, dividing it into small areas, finding the time taken to cross each area individually, joining the areas into all possible chains between the top of the hill and the house, and then finding which chain gives the smallest total time for the journey. The path so selected is absolutely the best and has been selected by what I shall call the " strategy " of the problem. (I shall use the words " strategy " and " tactic " throughout this paper in the particular senses defined, and with no correspondence to other usages, though in some cases our " strategy " will correspond to von Neumann's " Minimax strategy.")

Usually, of course, the traveller would not use so elaborate a method. A common method would be to make the selection in stages. He would first select a point about a hundred feet down to which he could get rapidly ; then, arrived there, he would select another point a hundred feet lower still to which a rapid descent was possible, and so on till he reached the house. This method I shall call a simple *tactic*, as contrasted with the previous *strategy*. The tactic differs from the former in that the tactic does not take into account the whole of the situation, but proceeds according to a criterion of optimality that is applied locally, stage by stage.

This example, of the traveller on the hill, is really more general and widely applicable than might at first appear. We can in fact replace the hillside by an abstract space and the expected elementary times t_i (on the elementary areas) by some function $f(P)$ of the points P of the space. At this level of abstraction the problem is then to find a curve C between the initial and terminal points, such that the integral

$$\int_C f(P)dP$$

is a minimum.

To see more clearly how the concept can be applied when the problem is not geometrical, let us consider an example of quite a different type. Suppose a specialist in vocational guidance has to allot n given persons to n given jobs, when he has already tested them and has made predictions (n^2 in number) of the " suitability " (on some scale) of each person for each job. His " goal " is such an assignment as will maximise the suitabilities *over the whole set.* Thus, it might happen that three people A, B, and C had the suitabilities shown in the Table for jobs I, II and III.

	I	II	III
A	9	10	4
B	5	8	4
C	3	2	1

An "assignment" (of people to jobs) is determined when we have selected three entries, no two being in the same row and no two in the same column.

Here the strategy would consist of computing the totals corresponding to each of the $n!$ possible assignments. In this example there are 1 × 2 × 3, i.e., 6 possible assignments; trials soon show that the best is that which gives A the job I, B the job II, and C the job III. This scores 18, and no other assignment scores more.

If n is large, the computations become prohibitively heavy; a possible tactic is then to proceed by first picking out the largest entry in the table, then cancelling out that person and that job, then selecting the next largest in the remaining $n - 1$ persons and jobs, and so on to the completion of the assignment. If it is applied to the table, then the score of 10 first determines that A is to be given job II, then the 5 gives B the job I and then C gets job III.

This tactic scores 16, little less than the maximum of 18. We see therefore that it may be possible to achieve fairly easily a score that is only slightly below the best when the best itself is quite impossible of achievement (as would have been the case in this example had n been thirty instead of three).

The same principle occurs in chess-playing. If, toward the end of a game, player A can see how to beat B in spite of all defences, then A will be following what I have called a strategy. Often, however, this perfect way to the goal cannot be perceived; then A looks for some move that will achieve a temporary or local advantage, such as capturing B's Queen, or covering the largest area of the board, or promoting a pawn, etc. Such a move is a tactic.

STRATEGY AND TACTIC.

Our next step is to see more clearly what is the relation between these two—to show them as derivatives of a single concept. Let us go back to the man on the hill.

Let us assume that by now he has discovered everything about the hillside, so that he now knows the true minimal time T_i necessary for going from every point P_i of the hillside to the house. This information he has conveniently schematized on his map by drawing a series of *isochronic curves* such that each curve joins all those places that are situated at the same (minimal) time from the house. Thus, the curve marked "5 minutes" would run through all those places from which the house can be reached in 5 minutes but not less.

Once the map has been prepared, a simple reasoning, borrowed from the calculus of variations, shows that, given any starting point, *the optimal path to the house is one that cuts every isochronic curve at right angles.* (Technically we may express this by saying that the optimal paths are geodesics in a variation problem and that the isochronic curves are the "transversal" of the problem.)

From the practical point of view, the introduction of the isochronic curves is not a mere artifice. In some problems a computation of the solution may be obtained easily if the path is computed backwards from the goal. Sometimes, though more rarely, it happens that computation of the isochronic curves is actually the quickest way to the solution—the most economical in the number of arithmetical operations. Thus, in the problem of assigning jobs we saw that

$n!$ sums involving $(n - 1).n!$ additions had to be performed; if, however, we follow a method derived from the considerations just given, the number will not exceed $n(2^{n-1} - 1)$, which is far fewer; for instance, if n is 12, the number of elementary additions falls from 5,269,017,600 to 24,564. Similar reasoning has been used by Hoffman to design codes of minimal redundancy.

The introduction of isochronic curves enables us now to see more clearly the relation between a strategy and a tactic. For if a point follows a path that is everywhere at right angles to the isochronic curves then it is also moving in such a way as to make maximal the instantaneous decrease of the remaining time—it is moving optimally according to the *local* conditions. In other words, if our man behaved as if acted on by a field of force deriving from a potential (which had the isochronic curves as equi-potential lines), then his path would be identical with that determined by the optimal strategy. It is now clear that once the isochronic curves are given, i.e., *once the map's projection has been changed to that of the really optimal metric, the distinction between strategy and tactic disappears.*

Classification of Imperfect Tactics.

Having considered the optimal path, let us turn next to consider the case of the path that is grossly non-optimal, to that, say of a stone rolling down towards the valley under the action of gravity. According to the laws of physics, the stone, at each moment, is falling in such a direction as takes it the longest distance down in the shortest time, when only immediately local conditions are considered. Thus the difference between the behaviours (or paths) of man and stone is simply a difference between the fields which direct them; the man's field is truly optimal, for it is based on the isochronic curves, and the stone's field is that of its crudest approximation—the Newtonian field of gravitation.

In addition to these two fields are others; what can we say *a priori* of their properties and of their values as tactics?

First they may be classified according to what I shall call their "span of foresight"; thus, if the man coming down the hill plans each next move according to the details of the next hundred feet he will do better than if he were to plan only over the next ten feet. The spans of foresight are here a hundred feet and ten feet respectively.

Should the span of foresight be equal to the distance from the goal, then obviously the tactic and the strategy become identical.

The second characteristic that is to be considered is the behaviour's "flexibility." Suppose the span of foresight is "100 feet below"; once the man has covered half this distance he may discover that his provisional goal was not the best, and that he should now take a different path for a different goal, again at one unit of foresight ahead. Clearly, in the strategy of the traveller with complete foresight the concept of flexibility plays no part, and neither does it at the other extreme—the case of the rolling stone (for the latter's steps are assumed to be infinitesimal, so that no smaller step is possible). It is in the intermediate degrees that the concept becomes important.

After these preliminaries, it will be seen that any goal-seeking behaviour may be classified on a scale of strategies and tactics, each one depending on a general function representing some measure of the distance between the present position and the goal. Thus, for the stone, the function depends on the present altitude above the bottom of the valley. Had the stone been a piece of iron and the goal a big magnet, the function would have depended on the object's present distance from the magnet. Other models would have led to other functions ; so we have many tactics, each depending on a single function. The complete specification, and full classification, are given when to this function we add the span of foresight and the degree of flexibility, the latter being conveniently measured by the minimal time at which the provisional goal may be replaced by another.

THE STOCHASTIC ENVIRONMENT.

What we have done so far is to show that the " strategy " is simply one of the tactics : it is that extreme tactic based on the best function as given by the isochronal curves. It is now instructive to show conversely (so close is the relation between them) that any tactic may be viewed as some sort of strategy. This is so if the time t_i taken in crossing each elementary area is not permanently constant, as we have assumed so far, but depends on other factors of which we know only the probability of their values. Thus one of the areas might be a marsh that is easy to cross when the weather has been fine but difficult to cross after rain ; if the traveller does not know what has happened prior to a *particular* trip, he can give only a probability to any particular " duration of crossing." Again, another area might be a lake, to be crossed only by a boat which may or may not be available, and so on. More generally we can assume that the elementary times t_i are not given fixed values but are given fluctuating values, depending on some random or " stochastic " process.

If now we apply the theory of inductive behaviour as defined by Wald on the Ville-von Neumann principles, we find that *the optimal strategy is just the simple tactic of attempting to do one's best on a purely local basis.*

To illustrate this thesis let us consider some well known examples. First consider that of the dog that wants to run to his master, who is himself walking steadily in a definite direction. If the dog is something of a computer it will perform an integration and will go directly to the place at which their relative velocities will enable them to meet. If the dog is not so clever it will continuously run directly towards where its master is at that moment. This second tactic is, of course, the simpler of the two, but is inferior if the master is moving uniformly. If, however, the master is making steps backward and forward in a totally random way, as if he were undergoing a Brownian movement, then this second tactic can be shown, by mathematical proof, to be actually *the best one possible.* The tactic has become the strategy.

Here is a second example. A number of lengths of telephone wire must be joined end to end to complete a long-distance line. Each length imposes some small but characteristic distortion a_i on the message. The overall distortion is the sum of the individual distortions, but by reversing a length before it is joined the distortion can be added positively or negatively. How should the lengths be joined if the total distortion, $\Sigma \pm a_i$ is to be a minimum?

If a hundred lengths are to be connected, the absolute optimum can hardly be achieved, for the number of sums that would have to be calculated (if all possibilities are to be explored) is prohibitively large. What is the engineer to do? In practice, he adds the lengths one by one, at each new addition adding the wire this way or that so as to make the sum as small as possible at that particular stage. This tactic has been found to give quite satisfactory results, its success, perhaps, depending on the fact that this tactic really is the best possible if the wires are provided, and have to be connected, one by one.

Other examples of this thesis—that the optimal strategy often consists of doing one's best on a local basis—is also used in Fano's method for finding an optimal code, and in Gavrilov's method for building up a switching system that will represent a given logical function at minimal cost.

Conclusion.

In this paper I have attempted to show something of what is implied by "goal-seeking" when the whole situation is more complex than that occurring in, say, a simple thermostat. It is clear that the further study of these situations will have to be made mathematically. It is also clear that much more development will be necessary on the purely mathematical side, for much of the necessary mathematics will have to be developed specially. To the mathematician many of the problems raised are new, and will need new methods.

In particular we need to know more about how much efficiency is lost when the span of foresight and the degree of flexibility are not optimal. The problem is not made easier by the fact that often the parameters do not enter the problem with random values, so the appropriate theorems will have to be stated in a somewhat unusual form.

The purpose of this paper, however, was not to enter into these technicalities but to show in a general way how the introduction of mathematics into this branch of psychology might itself be a worth-while tactic.

Summary.

When "goal-seeking" behaviour is considered in situations of more than the most elementary type, the problems that arise are related to those of strategies and tactics.

I have attempted to show that clear-cut principles are involved, capable of mathematical treatment.

It appears likely that among the factors of special importance are those of "span of foresight" and "degree of flexibility."

The case has also been considered in which the organism faces an environment that can be characterized only in terms of probability.

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BREAKING OSCILLATIONS IN SERVO SYSTEMS.*

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The present paper is concerned with some aspects of stability and of steady periodical changes in dynamical systems. After a brief survey of the classical theory due to Poincaré, I shall sum up some of my recent work relating to a certain class of systems not considered in that theory. It is, of course, assumed that this work is relevant to the main subject of this meeting; in fact, in the course of writing down these notes I was fortunate enough to be able to look (although far too cursorily) through Dr. Ashby's book, *Design for a Brain*, and have been struck by what appeared to me to be a remarkable parallelism between our lines of thought. The arrangement of the subject-matter has been avowedly influenced by this assumption of relevancy; however, I shall keep to my legitimate grounds as a physicist and shall leave it to you to fill in whatever "psychological" conclusions you may think justified.

The theory of dynamical systems is mathematical in its essence, and abstract reasoning cannot be dispensed with; what I can, however, and shall, avoid are the technicalities of analysis: those interested might refer to the papers listed below for a more mathematical treatment. First let me define the special words that will be used.

Concepts and Definitions.

A "dynamical system with n degrees of freedom" is anything which can be wholly described by a set of $n+1$ variables, one of which is the time, the others having any physical meaning. (If a living organism is to be regarded in this way we must include all those variables in both organism and environment that are necessary to make the behaviour determinate. In this paper I shall, of course, be considering systems of much less complexity.) The n variables can be made to correspond, in the usual way for graphs, to an n-dimensional space in which the set of values of the n variables corresponds to one, and only one, of the points of the space. As the variables change in value so will the point change in position. Thus the state of the system at a given time t is represented by a point in the space, the point at the extremity of an n-vector $\mathbf{x}$. The locus of this point as the time progresses is a "characteristic" of the system. (The "line of behaviour" of Dr. Ashby's terminology is almost identical, though somewhat more general; Poincaré's word is, however, more suitable when discussing systems of the type studied by him.) Such a representation of behaviour by a line is well known in everyday life—many a map of the Coronation, for instance, showed by a winding line how the "chain of events " of the day would occur. A " characteristic " represents the events in a dynamic system similarly.

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* A Paper read at the Annual Meeting of the Royal Medico-Psychological Association, held at Barnwood House, Gloucester, on 9 July, 1953.

(It will be convenient from now on to use the language of plane geometry, which, of course, applies strictly only to a system with two degrees of freedom ; but any proposition stated in that simple language can be easily extended to the general case.)

Any characteristic represents one solution of a certain set of first-order differential equations, corresponding to given values of the arbitrary integration constants. All the solutions of the set of equations yield a family of characteristics, and it will be considered that any curve of that family represents the behaviour of the same system, when starting from different " initial conditions " as enforced, at some given time, but not subsequently, by an external agency. If, at any stage of its free evolution, the state of a system is disturbed by an external agency enforcing for a moment new conditions and then leaving the system alone again, the representative point will be thrown off its original path to some new position, and will then go on describing the particular characteristic that passes through that position. These events correspond to what happens in a physiological or psychological experiment when a transient " stimulus " is applied. They would also correspond more generally to the experience of the psychiatric patient who has undergone some traumatic, but not persisting, disturbance.

We shall be particularly concerned with a system's equilibrium and steady (periodical) motion. (It will be readily seen that a steady (periodical) motion is akin to an equilibrium, for the system will encounter the same state, if not at all times, at least an infinite number of times at fixed intervals.)

A system is in " equilibrium " when its characteristic reduces to a point, that is, when the vector $\mathbf{x}$ does not change with time. When the characteristic is a closed curve, the changes of the system are, necessarily, periodic with respect to time.

Another important property of a system is its " stability." Suppose that a system is disturbed from its rest (or closed path) : it will start on a neighbouring characteristic of the same family, as explained above. If that characteristic tends to merge into the original one in course of time, then the original state (or closed path) is " stable " ; if, on the contrary, it drifts farther and farther away, the original state (or closed path) is unstable.

It is hardly necessary to point out that these two questions are of primary importance in the study of servo systems, whether mechanical, or maintaining vegetative homeostasis, or concerned in the many regulations implied by well co-ordinated and self-preserving " higher " activities ; for a system's stability is a major factor in determining how it will react to a transient signal or disturbance. There are, of course, other points of view equally important for the discussion of servo systems, for instance that of selectivity ; but to go into them would require a whole course of lectures, not a brief paper ; so it will perhaps be better not to touch on them at all.

For systems governed by equations of the type

$$\dot{\mathbf{x}} = f(\mathbf{x}),$$

where the f's are sufficiently well-behaved functions (*v. infra*), there is a very satisfactory theory of characteristics due to Poincaré and his school. Its main results are as follows :

PROPERTIES OF THE POINCARÉ SYSTEM.

(For precision it is best referred to by this name ; for convenience it may be thought of as being approximately a continuous system.) Its most important properties are, in general, those of its "singular" points ; these occur wherever the f's are null, i.e., become zero. They all correspond to well-known and commonly occurring features of behaviour. They can be classified, completely, as follows :

$$\text{Focus}\begin{cases}\text{stable.}\\ \text{unstable.}\end{cases}$$

$$\text{Node}\begin{cases}\text{stable.}\\ \text{unstable.}\end{cases}$$

Saddle point.
Vortex.

In a Poincaré system, every singular point belongs to one, and only one, of these six classes.

A graphical illustration of their main individual properties is given in Fig. 1. The behaviour of the system in the vicinity of any of these points can be easily understood if we regard the characteristics in Fig. 1 as showing the contours of a hilly country. Thus a node is a peak or a hollow, and a ball released in its

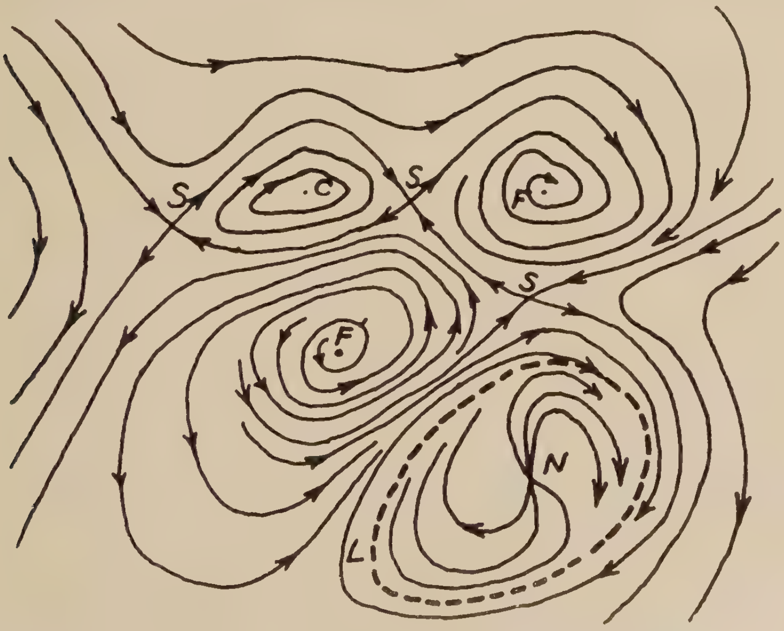

FIG. 1.—Example of a family of characteristics showing various singularities : C, vortex ; F, focus (stable) ; F', focus (unstable) ; L, limit cycle (stable) ; N, node (unstable) ; S, saddle point.

vicinity will roll away from it if it is a peak (corresponding to instability) (*N* of Fig. 1), or towards it if it is a hollow (corresponding to stability). Foci are also peaks or hollows, but the surface is nearly or quite level around them ; so at a focus, the ball will follow a winding path, away from a peak (F') or towards a hollow (*F*), each spiral closely approximating to a contour. Around a vortex (*C* in Fig. 1) it will follow a contour indefinitely (if there is no friction). Thus, foci are reached after an infinite time (if stable), or were left at time $-\infty$ (if unstable). Vortices, on the other hand, are related to a state of rest, and are surrounded by a continuum of closed paths, each path representing a periodic motion. According to our previous definition, the motions around a vortex are neither stable nor unstable, since the system, when displaced to a neighbouring path, neither drifts away from the original one nor tends to go back to it. All energy-conservative systems come within this case. However, in practice, when the system is subjected to repeated disturbances or "noise," this "neutral" stability looks more like instability ; for after each disturbance a new path is begun, and the observer sees only an aimless drifting.

The motion may also proceed from an unstable node or focus, or unwind itself from an unstable limit cycle. A limit cycle is always surrounded by an annular region where all paths tend towards the cycle or unwind themselves from it. In particular, if the cycle is stable (*L* in Fig. 1), the motion of the system tends to become ultimately periodic for all initial conditions interior to the annulus, and this limit is independent of the initial conditions. These limit cycles are *the only stable periodic motions* possible to a Poincaré system. In such a system, a limit cycle is always approached gradually, the characteristic never reaching it, strictly, in any finite time. This asymptotic approach contrasts with what I shall show later, in which an abrupt arrival is possible.

Lastly, a saddle-point (*S* in Fig. 1) is the equivalent of a pass in the hills, and is the only kind of singular point which can be crossed by the representative point.

It can be proved that a closed characteristic is bound to contain in its interior at least one singular point.

As time goes to $+\infty$, every characteristic must lead to one, and only one, of the following conditions :

(i) The motion leads to a stable node and stops there :

(ii) it leads towards a stable focus, reached after an infinite time has elapsed ;

(iii) it leads towards a closed curve, the limit cycle (e.g., *L* of Fig. 1), merging into it after an infinite time ;

(iv) it goes to infinity.

In the absence of any external agency exerting more than temporary action, a Poincaré system can therefore either proceed towards a state of rest (reached after a finite or infinite time), or proceed towards a steady periodic motion, reached after an infinite time, or, lastly, have a characteristic stretching to infinity in the phase space. Now, whatever the physical meaning of the variables $\mathbf{x}$, it can be safely assumed that they cannot exceed certain values without a destructive change happening in the system (at best, the system will, outside a certain region of the phase space, be governed by other laws ; but this means that it will be another system, and the original one may be deemed destroyed). The last possibility is therefore that the system proceeds to its destruction. These remarks conclude my survey of the main properties of the Poincaré system, but the last possibility—that it may proceed to its destruction—leads into the next development.

The System with "Memory."

In the systems considered above, the law of change depends only on the state of the system at the time considered (on the vector $\mathbf{x}$). This class, akin to Dr. Ashby's "absolute" system though not identical with it, is called *non-hereditary*. A system is *hereditary* (Volterra) if its behaviour at a given point of the phase space also depends on all the points previously occupied. It may also be considered as a system that has "memory," in the sense that some of its physical components have properties that depend on its past history. In the systems considered by Volterra, this "accumulated experience" of the system is expressed mathematically by a line integral taken along the path, and the governing equation is integro-differential, instead of being simply differential.

There are few physical systems where a close scrutiny does not reveal some degree of hereditary action; to take a simple example, the stiffness of a spring depends on the succession of temperatures to which it has been subjected, and even on the duration of the stress previously borne, whether the elastic limit has been reached or not.

The discussion of hereditary systems is usually a difficult problem, even in the simple case where the hereditary action is restricted to one single variable, and when it is assumed that the influence of previous states grows negligible when these recede in the distant past (Volterra's assumption of the "dissipation of hereditary action"); in more general cases, our present mathematical tools are quite inadequate. But the class of hereditary systems is of such importance that it is well worth while discussing even a particular case, for every new solution adds to our knowledge of the general behaviour of these systems. They are of particular importance in the living world, where most systems are of the type that cannot be considered adequately except in reference to their past history.

It has been pointed out that the classical theory outlined above is restricted to non-hereditary systems. More than that: of this class, it applies only to those systems that are governed by equations involving "well-behaved" functions. This vague term is used intentionally to stand for a set of precise technical conditions into which we need not go here, and whose general effect is to ensure a certain degree of smoothness in the representative curves or manifolds. The question now clearly arises, what happens when the functions are *not* well-behaved? The question is of great importance, for the common functions in the physical world are those of this second type, not those of "well-behaved" type; Nature, as Sir Isaac Newton pointed out, does not heed mathematical difficulties. Now given a discontinuous function, it is a well-known theorem that a continuous function can always be found which will fit the exact values of the given one, in a stated interval, with an error as small as desired. Results of experimental measurements can therefore always be expressed by a well-behaved law in the interval under study with an excellent accuracy, while the actual law may be of a different nature, and lead to unpleasant difficulties outside the interval in question. Our general theorems are valid only for the "idealized" case, and do not enable us to say that two characteristics, now infinitely near to each other, will remain so when the one is governed by a well-behaved, the other by a fractious, law.

PROPERTIES OF THE "BREAKING" SYSTEM.

It would be too ambitious to attempt a general theory valid for all fractious functions; but some particular classes can be considered. The one which will be discussed now is at the same time hereditary and discontinuous, and may thus suggest some ideas as to the behaviour of two different, and little known, categories of systems. We shall assume from now on that the hereditary action is concentrated on a curve or manifold which will be called the "boundary", and that its effect is to add a certain term, with alternate signs, whenever the representative point of the system touches or crosses the boundary. The system is thus alternately subjected to one of two well-behaved laws, corresponding to two different families of characteristics, say (R) and (S) (Fig. 2). The actual path of the representative point is made up of an arc R, followed by an arc S, then another arc R, and so on, all the changes occurring on the boundary.

In Dr. Ashby's language, the law of motion is governed by a step-function, the steps occurring on the boundary; his Fig. 7/8/2 is analogous.

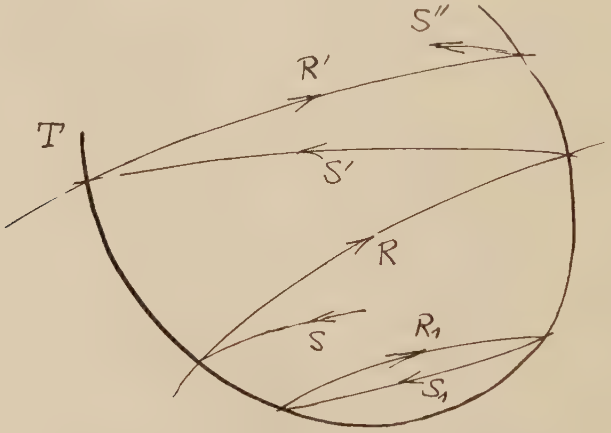

FIG. 2.—Phase plane containing paths of a breaking system.

Such a path can be closed; for instance the first arc S may cut the boundary at the same point as the first arc R, and the motion will then be $R_1S_1R_1S_1$ . . . as shown in the figure. Obviously, the period is here made up of two phases (R_1 and S_1) which may differ greatly in character; thus, in one case of great physical importance, the breaking of waves on a shore, one of the phases is a " jump." It is with this instance in view that I called the class of oscillations under discussion " *oscillations de déferlement*," the English for which I believe to be " breaking oscillations."

To grasp the properties of this new type of system another method of representation is advantageous. You may find it unusual, but a little practice soon makes it familiar. Let the characteristics of each of the two families be numbered, so that each point of the phase space is determined by two numbers : that of the R-characteristic which passes through it, and that of the S-characteristic which also passes through it. Take these numbers as new rectangular co-ordinates η and ξ respectively. In the η, ξ-plane, the characteristics R and S will become vertical and horizontal lines, the boundary T will be transformed into a certain curve τ, and the path of the system will be made up of vertical and horizontal segments, intersecting on τ. The closed path of Fig. 2 (R_1S_1) will obviously correspond to a *double point* of τ, where two branches of that curve intersect ; one of these branches will be repulsive (⊕) with respect to a given family R (or S), and the other will be attractive ⊙. Fig. 3 shows that the necessary and sufficient condition for the periodic solution to be stable is that the repulsive branch should have the greater slope with respect to the family axis.

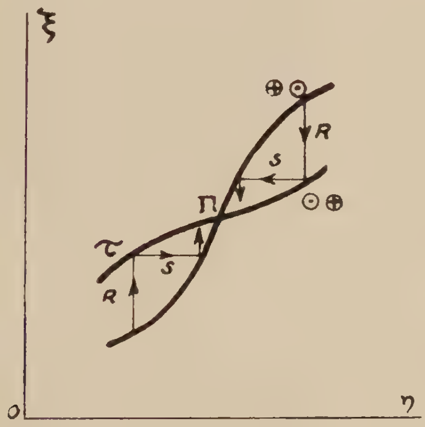

FIG. 3.—Transform of the phase plane of Fig. 2 to the plane of η, ξ. Π is the double point corresponding to a stable closed path, e.g., to R_1S_1 in Fig. 2.

The oscillations represented by a closed breaking characteristic such as this one (R_1S_1) may be called " of the first kind." A " second kind " will be that where the cycle is made up of four arcs, two of each family, and so on. These higher kinds cannot occur if no two characteristics of one family intersect within the boundary, i.e., if there are no interior singular points. Similarly, if there is at most one singular interior point of each family, the periodic solutions may be either of the first or of the second kind, and so on. Fig. 4, though somewhat complex in the diagram, represents a simple system with pentagonal boundary. It is purely theoretical, but has been constructed to show some of the elementary properties with special clarity. One family of characteristics is made up of straight vertical lines (considered as degenerate parabolae with no interior singular point), the other of hyperbolae (having an internal saddle point at O). The behaviour of the system can be found simply by starting at some initial state and following the appropriate characteristic, changing to the other family every time the boundary is reached. Thus possible behaviours are: **(A)** If started at A (in the lower quadrant), it goes through B to C; here it falls just below the critical line, so it turns down to D (instead of going eventually up to B'); after going to D, it converges to the cycle Π_1', Π_2', Π_1', . . . **(A′)** If, however, it is started at A', it converges to the cycle Π_1, Π_2, Π_3, Π_4, Π_1, . . .

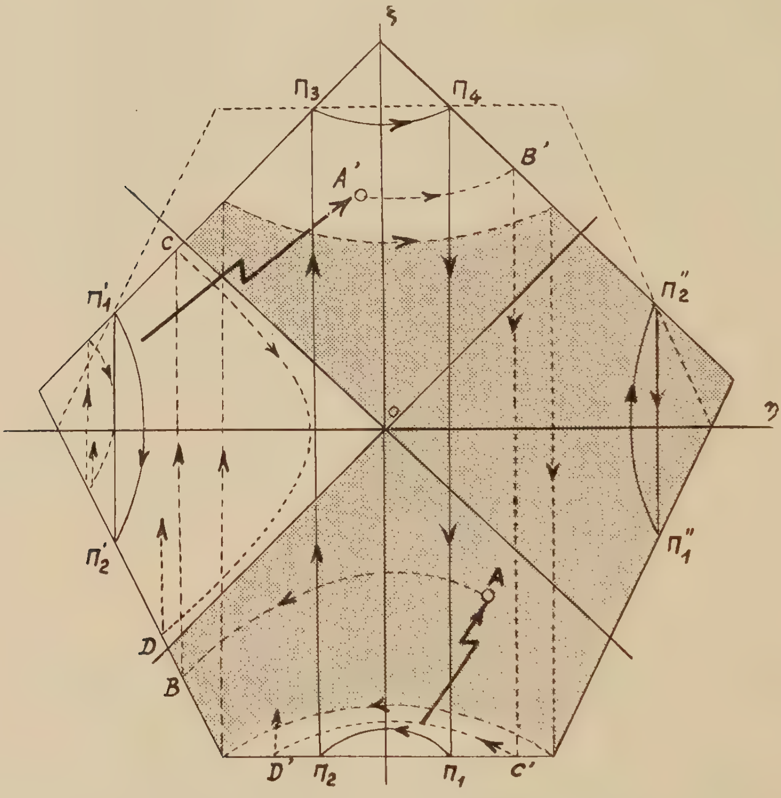

FIG. 4.—Phase plane of the breaking system that is realised in Fig. 6 (*c*). It shows closed paths of the first kind: $\Pi_1'\Pi_2'$ (stable) and $\Pi''_1\Pi''_2$ (unstable) and of the second kind: $\Pi_1\Pi_2\Pi_3\Pi_4$ (stable).

There are two steady motions of the first kind (Π_1', Π_2' and Π_1'', Π_2'') and one of the second (Π_1, Π_2, Π_3, Π_4). The rules for stability are the same as in the simple regular case, applying to each set of boundary points concerned. So much for the general description. I shall now point out very briefly some of the peculiar properties of the systems we have been considering.

PECULIARITIES OF THE "BREAKING" SYSTEM.

The occurrence of interior foci or nodes obviously excludes the possibility of any periodic motion, since they cannot be crossed an infinite number of times, but there may well be a node on the boundary, and in that case a periodic motion of the first kind will exist, stable if the node is attractive, as shown in Fig. 5. It is readily seen that the steady motion is reached after *one single discontinuity*, whatever the initial conditions. A breaking system with a node on the boundary reaches its steady motion almost immediately, not asymptotically as was the rule in the classical case.

Now this is rather remarkable, and worth while checking experimentally. In a previous paper I have shown that the multivibrator circuit, well known in electronics, may be considered in a large number of cases (under not very restrictive conditions) as a breaking system with both families having a node on the boundary (a complication which makes no significant difference). And in fact, oscillograms (Fig. 6(*a*)) of the building-up of the steady periodic motion in such circuits show that the amplitude and period are reached completely at the second " flip," just as predicted by the theory.

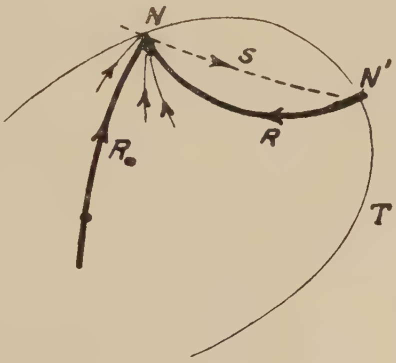

FIG. 5.—Phase plane of a breaking system that possesses a node on the boundary.

Another noteworthy property relates to systems with saddle-points: such systems may display a number of steady states of the first and the second kinds, not separated by any unstable regions; on the occurrence of a disturbance of sufficient force, the system will jump suddenly from one way of behaving (one stable path) to another, the second way of behaving being perhaps quite different from the first. If disturbances are recurrent and invisible, the system will give the impression of behaving at random when it is really stable and quite able to continue steadily in one path once the disturbances cease. The possibility is predicted in Fig. 4. If it was moving steadily and cyclically between Π_1' and Π_2' (on the left) and a disturbance (shown by a solid zigzag line) threw the system suddenly to state A' (in the upper quadrant), then it would go to the cycle Π_1, Π_2, Π_3, Π_4, Π_1 . . . around which it would circulate permanently.

The same phenomenon can be demonstrated in an actual model. Its details need not be referred to here as we are interested only in its behaviour. Its phase space is similar to that shown in Fig. 4. Fig. 6(*b*) shows two of its cycles (photographed successively) as they appeared on the recording oscillograph. A disturbance, applied between the two exposures, has thrown it

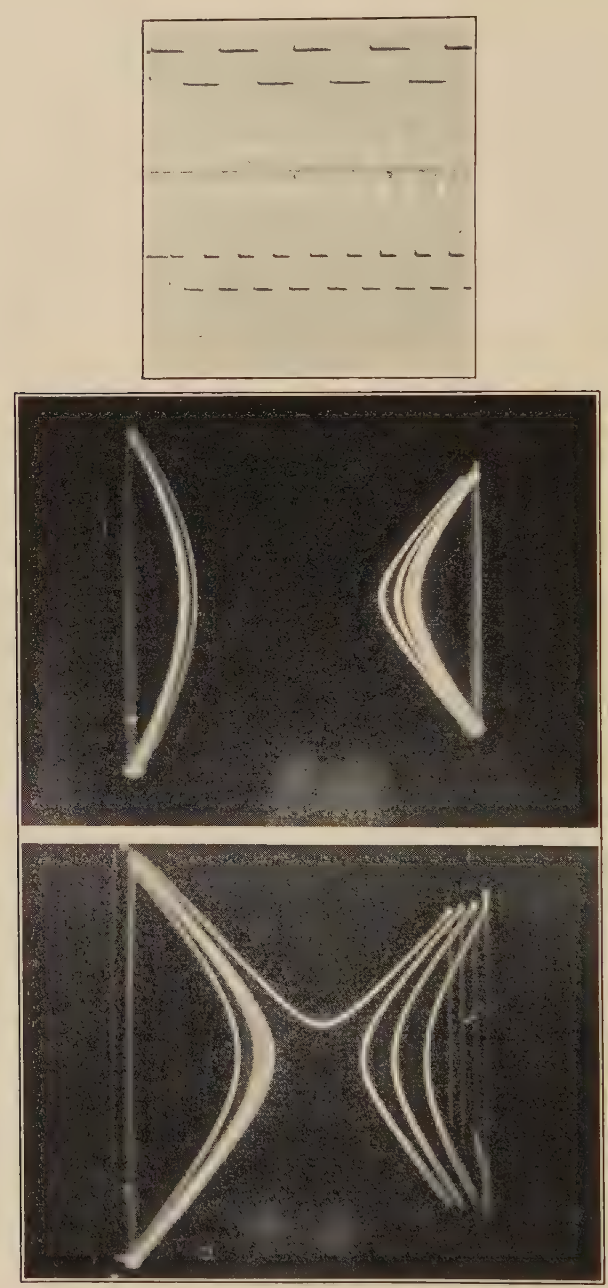

FIG. 6.—(*a*) Two oscillograms of a multivibrator as it starts. (Time goes from left to right.) Notice that the steady motion is reached at the second oscillation, there being no gradual build-up, in contrast to L of Fig. 1.

(*b*) Oscillogram of the phase plane for a system similar to that of Fig. 4, but with different slopes at the boundary. It shows two stable oscillations of the first kind.

(*c*) (As *b*, but the boundary is now as shown in Fig. 4). It shows two oscillations of the first kind. The system was started in that on the right side; but the oscillation was unstable, so the point drifted away, then jumped to the other cycle, and finally settled there.

from one cycle to the other. (The mechanism was modified for 6(*b*) to make both cycles stable.)

These "breaking" systems are much richer in properties than the basic Poincaré (continuous) systems. Fig. 6(*c*), for instance, shows a property that is impossible in the Poincaré system yet is probably common in systems with discontinuities. It is obtained from the system shown in Fig. 4. (In contrast to 6(*b*) the right-hand cycle is now unstable.) If such a system is started in the unstable cycle on the right it will for a time seem to be following a regular cycle (Fig. 6(*c*), on the right); then, *without any disturbance from the outside,* it will suddenly jump to another way of behaving, and will settle down to the steady cycle on the left. The possibility can thus both be predicted, in the theory of Fig. 4, and demonstrated, in the model whose behaviour is recorded in Fig. 6(*c*).

I do not feel that any elaborate conclusions would be in order, especially as I am a physicist encroaching on the realm of neurophysiology. The general impression I have tried to convey is that complicated systems can do quite unusual things while still being orderly and determinate. If, as often happens, a system can undergo *dis*continuous changes, then the behaviour of the system can be surprisingly "original", making the behaviour look disorderly while it is actually stable and normal. When faced with a behaviour which strongly differs from what one considers to be normal, one generally looks for an external agency; but it might be wise, sometimes, to consider whether the internal properties of the system are not really more complex than was assumed at first.

SUMMARY.

Our understanding of the dynamics of the brain must be built up stage by stage, the elementary and simple being clearly understood before the complex is attempted.

A description is given of the main properties of the system whose variables are continuous; and a further study is given of the properties of the system that contains a few discontinuities ("breaks" or step-functions).

Systems in which "breaks" can occur show some interesting properties, three of which are described. Particularly noteworthy is the fact that such a system, even if strictly determinate and within constant external conditions, can change suddenly from one way of behaving to another, apparently spontaneously.

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THE APPLICATION OF CYBERNETICS TO PSYCHIATRY.*

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At the moment, cybernetics cannot point to any established triumph for, as a science, it is very young and is being applied to psychiatry in few laboratories. Nevertheless, I hope to show that there are good reasons for thinking that its relation to psychiatry is close, and that its application will eventually yield a rich harvest.

Cybernetics can hardly fail to interest the scientifically minded psychiatrist, for it studies just those functions that are peculiarly "of the brain." It asks such questions as: how much information has the brain received ?, what combinations did the signals form ?, what memories are relevant ?, what pattern of action will be adaptive ? It studies switching, co-ordination, and integration—processes to which all the other cerebral processes are subsidiary. I propose, therefore, to review those branches of cybernetics that are likely to be applicable in practice, ignoring those branches, however attractive, that have no immediate prospect of application.

In one other respect I shall have to ask your co-operation. Cybernetics uses, basically, the methods and concepts of physics. These concepts have the great advantage of being precise and, above all, free from ambiguity; but they have the initial disadvantage of treating biological matters from a point of view rather different from that used traditionally. To master the subject, therefore, one has to learn to translate one's concepts from the familiar psychological to the unfamiliar physical. For this reason I shall have to ask you to see some of the old facts from a new angle. I hope to show that the new angle is worth achieving, for some subjects that previously possessed only obscure and ill-defined concepts can now attain an altogether new standard of objectivity and precision.

Perhaps the most fundamental advance made by cybernetics has been the discovery of exactly what is meant by a "machine." I don't want to start a discussion of whether the brain is "only" a machine, for that would lead us astray. But we do, as practical people, often study the mechanistic *aspect* of the brain; and so long as we are studying that aspect we must, if we are not to contradict ourselves, use concepts that are appropriate. Until a few years ago, no one quite knew what the word "machine" implied. We knew intuitively that *some* limitation was implied, but no one knew what; and much rather aimless argumentation raged round the question whether a machine could, or could not, show certain forms of behaviour. The matter is now much clearer.

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* Read at the Annual Meeting of the Royal Medico-Psychological Association, Gloucester, July, 1953.

We know that the essential feature of a machine is that, as a physical system, it is closed to "variation", that is, to information and noise. It is becoming evident that "information" is to complex machines what "energy" is to ordinary physical systems. When the concept of "energy" achieved full accuracy, just about a century ago, almost every branch of physics benefited and great advances followed rapidly. It is not impossible that the concept of information may be equally fertile in the study of complex mechanisms and the brain.

Some of the elementary applications of cybernetics to psychiatry are now well known and my reference to them can be brief. Well known, for instance, is the importance of feed-back, that is of circularity in action, and of stability. Such matters must inevitably concern the psychiatrist; for whoever deals with such highly dynamic systems as human beings will always find that questions of stability are of high importance. There are plenty of interesting topics here. There is not time for me to develop the subject fully, so I will merely pick on one or two facets of the subject for illustration. Take, for instance, the question: can a system be "over"-stable? The answer is undoubtedly "yes." The over-stable system is in general too rigid, responding to the events around it with insufficient amplitude. If the over-stability occurs in some *portion* of a dynamic system, then it tends to lose its effect over the other parts and to become functionally *less* effective in the whole action. This is due to the fundamental law that when a whole system is composed of a number of subsystems, the one that tends to dominate is the one that is *least* stable, the one that is nearest to instability. This statement is capable of mathematical proof and holds over all mechanisms, whether built of cogs, or neurones, or relays. As a simple illustration, consider the relations between a flock of sheep and the dog that guides them. The flock is driven this way or that by the dog's movements; and equally the dog's movements are determined, perhaps through a shepherd, by the way the flock moves; so flock and dog form a whole, with feedback between the two parts. Now, regarded simply as a physical variable, the flock is undoubtedly the *more* stable in its movements than the dog. To see that this is so, examine their respective tracks after they have gone past. We shall find that each small deviation of the flock's direction has evoked a much larger deviation of the dog's, for he goes far out to drive the flock back. Thus, in their movements, the dog is an amplifier, the flock a diminisher. The dog is thus the *less* stable; and it is the dog that determines the direction of the whole. *The one nearest to instability rules.*

Another example is given sometimes by a family with a neurotic member; for the neurotic member may keep the whole family in a ferment while the more normal members are inconspicuous. And the same principle must apply in the brain, where, if any part or subsystem should become less than normally stable it will exert more than the normal degree of influence on the brain's activities. Conversely, should any part become excessively stable, that part will be unable to co-operate adequately in the activity of the whole. *Stability*, then, *can be excessive; its penalty is loss of control.*

The opposite fault, instability, is, of course, well known. What is not always appreciated is that the conditions under which instability appears are often sharply bounded and critical even in a system in which every part varies continuously.* So if some factor affects stability, and there are few that do not, we should not assume that a slow and continuous variation of this factor will necessarily produce a slow and continuous change in the system's behaviour : on the contrary, *every dynamic system is potentially explosive*—that is, likely to develop a runaway. The conditions that this will develop are usually bounded sharply. So we would expect the change from stability to instability to be sudden, and out of proportion to the small change in the evoking conditions. These facts are true universally, and are quite independent of the particular details of the particular mechanism. They are equally true whether the mechanism is electronic, or neuronic, or hydraulic, or composed of cogs and rods. They are therefore necessarily true of the brain.

More can be added. Once a runaway has started, a mere holding of the external conditions constant is, in general, insufficient to stop the runaway. Even a return of the external conditions to the values that originally gave stability will usually be insufficient. Usually a runaway can be stopped only by a gross change of other variables. The approach of instability is often heralded by some form of oscillation. Observation of this may enable us to predict that instability is developing ; it may enable us to take steps for its prevention. These facts should surely find application in psychiatry.

So far I have considered the brain only as a single, complete, mechanism ; but cybernetics has forced us to consider the type of mechanism that might be called " statistical " : that is, a machine composed of parts each of which is an ordinary, determinate component, but a machine in which the components are so many that a vast amount of minor variation occurs and in which the assembly is so large that much of it is also arranged at random. Such a system has a good deal of internal freedom, and its behaviour will show laws that are valid only statistically : we can say what it will *probably* do but not what it *will* do. It will be law-abiding in its general tendencies but not in its details. The cerebral cortex may well be such a system.

We are, in fact, beginning to realize that the simple little neuronic structures that we used to imagine in the cortex, with one neuron doing this, and another doing that, with, in the very " complicated " forms, a third intervening, are ludicrously inadequate. They don't give even a first approximation to the real state of affairs. The modern calculating machine has taught us to think much bigger, though the largest of these is far below the mammalian brain in complexity. I cannot do better here than quote Lashley, who is describing our present knowledge and ideas :

" . . . theories of neuron interaction must be couched, not in terms of the activity of individual cells but in terms of mass relations among the cells. Even the simplest bit of behavior requires the integrated action of millions of neurons ; . . . I have come to believe that almost every nerve cell in the cerebral cortex may be excited in every activity. . . . Differential behavior is determined by the combinations of cells acting together rather than by cells which participate only in particular bits of behavior. The same neurons which maintain the memory traces and participate in the revival of a memory are also involved, in different combinations, in thousands of other memories and acts."

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* The paper by Dr. Vogel treats this matter in more detail and gives examples.

Lashley's picture is, in my opinion, far more realistic than any yet proposed. It recognizes that while there are systems like the typewriter, in which each part is of the same order of size as the whole, there are also systems, such as that of Great Britain, regarded as an economic machine, in which the parts are almost invisible when viewed against the whole. It recognizes, in neurophysiology, that even a minor action by a person is the outcome of almost uncountable neuronic activities in almost unimaginable complexity. Have I exaggerated a little?—there's no harm in that: at the moment our chief danger is that we will go on thinking too small, hanging on too tenaciously to our old habits. To-day, a resolute megalomania is a virtue; for we *will* have to change our ways of thinking about the brain—the new concepts are too big to be obtained from the old by a mere modification.

To show how profoundly the new views affect our thinking about the brain I will take as example the storage of memory and the question of its localization. (I say the "storage" of memory, for memory in all its aspects is too large a subject to be discussed now.) The word "memory" is often used to refer to the power of the *reproduction* of learned material: can the subject repeat the nonsense-syllables he learned yesterday, or can the patient repeat a text learned at school? This power of reproduction seems to be something of a by-product of the brain's activity: the not very intelligent parrot can do it quite well, and the magnetic tape-recorder can do it so much better than the human being that evidently the brain uses some essentially different method. More important in the brain, though less obvious, is the type of memory shown when a certain behaviour that has changed persists in its changed form. "Once a bicycle-rider, always a bicycle-rider"; so long as the skill persists, the person is showing memory, though he may perhaps be quite unable to recapture the feelings he had in the days before he could ride. This is a memory that shows in action rather than in recitation. It is often unconscious.

A good deal is now known about what sort of physical basis such a memory must have. Let me take the points in turn.

Its physical basis must be quantitatively suitable: it must have sufficient capacity. This capacity is measurable; and no mechanism of capacity K can carry a memory of information-content greater than K. Now an adult's memory capacity is very, very roughly about a thousand million units, so whatever the physical basis may be, it must be capable of providing that capacity.

In what material form is this capacity to be provided? In answering, we must remember that most elementary components, whether mechanical, or neuronic, or physico-chemical, carry only a unit or two on each component. Thus a reverberating neuronic circuit, that can be either at rest or fully excited, can carry only one unit, one *bit*. Suppose that our brains did in fact use such circuits for carrying our memories, and that an average circuit was composed of three cells. It would then follow, by simple arithmetic, that about a third of all our cortical cells would have no function other than to be set once and then to remain unchanged. This would be most wasteful and inefficient.

For this, and for similar reasons, a number of workers have examined the possibility that memory might be carried on much smaller structures, on the ultramicroscopic, or even on the molecular. Though there is as yet no certainty, physical considerations make it likely, in the opinions of Pauling and of von Foerster, that the essential change in memory occurs on structures of about ten to forty Ångstrom units, a size that would allow millions to occur in every nerve cell.

Is there anything against this? Before we reject the suggestion off-hand we should remember that the gene has about this size. The resemblance may not be as accidental as it seems, for any memory-basis in the brain has to subserve a function that is strikingly similar to that required of the gene during evolution and embryogenesis. Each has to be stable over long periods of time, and each has to be able to change to at least one other state. Each, too, has to be able to affect the processes that go on around it without itself being destroyed by them. From the point of view of information and control, the genes are simply the first message the mother gives the child: they are the memory-basis, in the mechanisms of heredity, for the information which one generation passes on to the next. Since the functions are so similar, we should not be surprised if their underlying physico-chemical bases prove to be similar.

We are thus led to a view of the brain whose memory-traces are: very small in size; scattered profusely over the cortex; and far too numerous to be arranged and controlled individually. We are thus forced to reconsider the questions of what we mean by the "localization" of such traces. When a system is small and simple, the localization of function within it is also simple. Thus, when I press down the key of the letter "S" on a typewriter, I can see that the typewriter's response among the levers is sharply limited to a certain few. These levers "belong" to "S" in a way that the other levers do not. "S" is here clearly and unambiguously localized. When, however, the system becomes very large, so that the component parts are incomparably smaller than the whole, this simplicity disappears. Thus, suppose we were to ask, is Britain's brewing industry localized? Two answers are possible. If we ask the exciseman he will reply: Every building in my district either is or is not in the brewing industry; of course brewing is localized. On the other hand, if we ask the geographer he will reply: No county in England contains the brewing industry; brewing in England is not localized. So the exciseman and the geographer hold exactly opposite views, and both of course are right. What allows this difference is that in a large system, such as a country or a cortex, the properties of the whole can be very different from those of the parts.

What this means in the cortex is that it is quite possible to have traces that are localized in the sense that each individual trace exists in some definite place in the brain, and that are also not localized in the sense that the whole set of them are not collected together in a small, anatomically recognizable region. This is what the modern statistical view of the cortex implies. It implies that the memory-traces that underlie each reaction are multiple, probably very much so, and that the individual traces are scattered over the cortex as widely and with as little apparent order as the industries of England are scattered over the counties.

This possibility was considered by Lashley as far back as 1929. He rejected it at the time, not because it was incompatible with the experimental and clinical facts, but because it seemed bound to lead, in the cortex, to chaos. For consider what this localization implies : there will be free intermingling of all the groups of memory-traces belonging to all the learned reactions, and this intermingling will take place in a network of neurons that is, histologically, rich in cross connections. Lashley was not alone in thinking that such a network could end only in chaos. Nevertheless, there is evidence, which I have given in *Design for a Brain*, to show that suitably arranged corrective feedback is capable of ensuring automatically that the patterns that develop are not chaotic but orderly and integrated.

We have now come to that process that is most peculiarly " of the brain " and of particular interest to the psychiatrist : the process of integration. What does it mean, in purely objective terms ?

Sometimes we use it descriptively, as when we say, after a pianist has played a piece of music correctly, that the various movements of his fingers were integrated. This aspect of integration can now be defined with full objectivity and precision. Sommerhoff, in his *Analytical Biology*, and I have come independently not only to the same opinion but to the same definition. We find that in any activity variables can be divided into the essential and the non-essential, and that in all cases the presence or absence of integration corresponds to whether the essential variables are or are not held within given limits. So far no exception to this rule has been found.

The word " integration " can also be used to refer to the success with which a number of parts are joined or related to form a whole so that the whole produces some desired behaviour. How the component parts of the nervous system are modified during learning so that the whole shall produce integrated rather than chaotic behaviour has been a major problem in physiological psychology. As Sommerhoff puts it : " The fundamental problem . . . is to discover how the behaviour of myriads of blind, stupid, and, by inclination, chaotic atoms can obey the laws of physics and chemistry, and at the same time become integrated into organic wholes and into activities of . . . purpose-like character."

The principles that govern the self-integrating mechanism are now well known, and prove to be essentially simple and straight-forward. Of course, the machine that embodies them has to be a little unusual, but not more so than any other machine that undertakes a special job. Let me sketch the method.

It depends on the fundamental law, true for all mechanisms, that a whole can rest at some state, be " in equilibrium," only when every one of its parts rests at its component of that state. This means, more picturesquely, that every part has, as it were, a power of veto, and that the whole can be in equilibrium only if *every* part is in equilibrium in respect of its own conditions. So if one part is built to allow equilibrium only when the other parts achieve certain conditions, then the *whole* will behave as if hunting for those conditions. In the living organism, the method would imply that there would have to be a certain basic structural form and a certain basic method of functioning.

The basic problem (see the Figure) is as follows: There is an environment and, interacting with it through receptors and effectors, a cerebral cortex. The environment has some action, for good or evil, on the organism's essential variables (E.V.), which must, if the organism is to survive, be kept within certain "physiological" limits. The cortex has various possible modes of behaviour, and the organism's problem is to find, given a particular environment, a mode of behaviour that shall so act on the environment as to make it keep the essential variables within their limits—satisfy the organism's basic needs. This can be achieved automatically if, and only if, E.V. (in the Figure) allows some random variation from a source *V* to pass along *U* to the cortex, the relation being such that the variation shall be allowed to pass when, and only when, E.V. is outside its proper limits—not conversely. The system is then, like the homeostat, self-integrating.

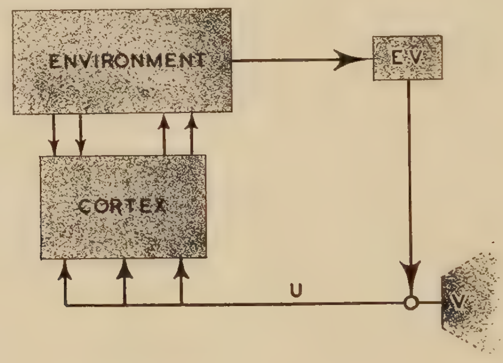

Figure.

Some further identifications between this purely functional diagram and the nervous system's anatomy can now be made. Cortex and environment have already been marked. What of the essential variables E.V. ? At present their localization in the brain is not known with certainty, and further research will be necessary; but it is obvious that sites worth considering would be the medulla and the hypothalamus. Enough is known to make these sites by far the most likely. The site of *V* is not important, for Brownian movement would provide an excellent source of the variation required, which, you will notice, need not be in any way systematic or specially designed. So *V* could be small, perhaps even of molecular size. It won't be found until specially looked for. The channel *U*, however, must be quite large, for it must carry *V*'s effects over most of the cortex. One thinks naturally of a tract like the mammillo-thalamic, that goes on to project over the cingulate gyrus, and one thinks too of the periventricular fibres that go to the dorso-medial nucleus of the thalamus and on to the frontal cortex; but these matters are not yet settled; they offer an exceptional opportunity to any worker who likes relating the functional and the anatomical.

So much for the modern view on how the cortex adapts to the environment. Next we can consider what will happen when the mechanism goes wrong.

For simplicity, we can consider first the limits that determine what values the essential variables E.V. will seek. These limits are set by heredity, and should correspond, in health, to the conditions that the organism must achieve if it is to live successfully. If they are set by heredity at a wrong value the organism will actively seek that wrong value, perhaps to its own destruction. Such an abnormality will, of course, not be common, for it would be eventually lethal and subject to rapid elimination under natural selection. Such does, however, occur, from time to time. A child is sometimes born congenitally devoid of the normal reflexes that protect him against injury: he is unable to feel pain, and he injures himself seriously and incessantly. Such a child, studied scientifically, should show some abnormality at the site of E.V. The mental defective who is self-mutilating, too, may be abnormal in the same way, and anatomical and histological studies of such cases should be most instructive.

Another abnormality that would spoil the power of adaptation is failure along the tract U. Along this channel comes the flow of variation that will force the patterns in the main cortical network to change when it is behaving in a non-adaptive manner. U can be at fault by transmitting either too little or too much. If transmitting too little, say by being cut by a tumour, or by a destruction of V, we would find that the cortex would be unable to change from one way of behaving to another. Having made a wrong action it would tend to persist in it, and we would remark that it was lacking in originality and initiative. Contrast this with what would happen if U was to carry too much variation from V. Now we would see just the opposite: a restless system ever on the change, actively trying one new behaviour after another, changing merely for the sake of change. The two types remind one somewhat of melancholia and mania, though whether these psychoses are really due to such a fault must be left for future research. The investigation should not be unduly difficult, for both the site of the abnormality and its effects on behaviour are rigorously predictable.

Another prediction that can be made with some confidence comes from the fact that the cerebral cortex is large and that any particular action depends on the sum, or average, of a large number of elements. In such a case, the accuracy of the action taken will depend, by a well known statistical theorem, on the *number* of the elements contributing. If the number should become diminished we would expect to see the error increase, and the amount of increase can be predicted. We would expect a gross cerebral lesion, not to abolish the learned reactions totally but to lead to an increased error in all the activities shown, so that, for instance, the patient's writing would become more shaky, his aim with a shot-gun more erratic, and his judgment more capricious. The prediction approximates to what is commonly seen, but here again research is necessary if the matter is to be tested stringently.

At this point I would like, if I could, to say something about how this new knowledge can help towards the development of more active and efficient methods of psychotherapy. Unfortunately, as you can see, this advance from the mechanistic basis of brain function has a long way to go before it can develop concepts and complexities adequate to represent, or to explain, the complexities of human neurosis. Nevertheless, there are some aspects of this work that seem encouraging. For instance, the psychoanalyst cannot, I think, be other than interested when he hears that this work strongly suggests that all cortical adaptations occur only on a basis, and under the direction, of more primitive and simpler forces. The forces, represented in the Figure by the essential variables E.V., are affected by the external world, the environment, only by being moved into, or out of, the normal physiological state. They receive no detailed information about the environment and they undertake no detailed activity, leaving the details to the cortex. They simply allow or disallow. Do the essential variables, seen by the mechanist, correspond to the basic instinctual forces seen by the psychoanalyst ? This work is too recent for me to hazard an opinion, but it seems to me that a study of the relations between these two concepts might well lead to advances in both sciences.

Another possible application to psychotherapy is given by certain recent work in cybernetics which has shown the fundamental importance in any complex mechanism of those combinations that are "self-locking," that is to say, of those combinations that, once formed, are no longer accessible to the influences that would unlock them again. We might, in order to have a definite example, call this the "problem of the oyster": the oyster, on receipt of signals of danger can shut quickly, but, being shut, cannot receive signals of safety. So every oyster tends to be self-locking in the shut condition. Oysters have long since evolved methods for getting themselves open again, but such a power does not exist generally. Often such a self-locking property leads to serious disorganization. The circulating disorder of the calculating machine is of this type, and it seems not impossible that the psychoanalytic "complex," as a portion of the psychic structure that is not accessible to those influences that would modify or re-educate it, may be of this type. I need not go further into the matter now: what I want to make clear is that the methods of cybernetics may be applicable here, and may be able to help in the task of breaking up the unyielding complex. Here is a field that might well attract the research worker who would like to develop psychoanalysis by making its basic concepts less metaphysical and more biological. Cybernetics offers the possibility of a psychology that recognizes to the full the richness and complexity of Man's strivings, while being based on concepts that share the objectivity and precision of physics. You will see that I do not regard psychoanalysis and cybernetics as being in the least incompatible.

Finally, I would like to discuss a possibility which seems to me to offer the best hope of all of understanding the aetiology of the psychoses, especially that of the so-called "functional" psychoses. Up to this point we have been considering the behaviour, normal and abnormal, of the basic adapting mechanism shown in the Figure. Such a mechanism, however, almost inevitably requires ancillary mechanisms, working to maintain the main system in a condition of optimal efficiency. We know, of course, quite a lot about the brain's optimal conditions in the elementary variables of oxygen supply, *p*H, ionic conditions, and so on; but we know as yet only a little of its more complex and subtle needs. These may show in a variety of ways not obviously related to the disturbances that their vagaries may cause. It is very likely that ancillary mechanisms will not only exist but will also be somewhat complex, for the cortex has not one but several optima, with different working conditions corresponding to different situations. Thus on one occasion the cortex may have to deal with a sudden and brief, but very dangerous, emergency, with speed of action as its most desirable quality. On another occasion it may have to deal with a mild, long drawn out difficulty for which the most desirable quality is the ability to handle relationships of great complexity. On yet another occasion its optimal action may be simply to leave well alone ; and on another occasion its optimal action may be to attack with the utmost violence. Each style of behaviour corresponds to a " temperament " ; and the cortex must be able, on different occasions, to act with different temperaments. The change from one temperament to another must, in a mechanistic brain, be due to the change in value of some parameter. We see therefore that the brain, if it is to be well equipped with a variety of temperaments, must possess ancillary mechanisms capable of setting the parameters of its action to a variety of values. This deduction is not surprising, for it has long been known that the autonomic has two main styles of behaviour—the sympathetic, adjusted for vigorous action, and the parasympathetic, adjusted for rest and digestion. The body thus has an ancillary mechanism, the autonomic, that can adjust it to either of two optima. Is it not likely that the cortex itself should have its own ancillary mechanisms, suited to its own needs ?

If this were so, we would expect these ancillary mechanisms to have their own faults and disorders, especially since the human brain is, on the evolutionary scale, a recent development. Suppose, then, that one of these ancillary mechanisms became faulty while the cortex itself remained healthy : we can predict something of what we would see in the patient's behaviour. We would see that the *details* of the patient's behaviour were essentially normal, for the details were determined by an essentially normal cortex ; but we would find that the general tenor was essentially abnormal, a caricature of some recognizable temperament. In other illnesses we sometimes see similar caricatures ; in exophthalmic goitre, for instance, we can trace the characteristic, though distorted, pattern of the person who is alarmed and alert. In disorders of the cortex's own ancillary mechanisms we would similarly see caricatures of the common temperaments. Thus we might see the healthy person's ability to think along new and original lines exaggerated to the incomprehensible bizarreness of the schizophrenic. We might see the healthy person's ability to think at great speed in an emergency exaggerated and distorted to the ideational flight of the maniac. We might see the ability to take things calmly exaggerated to the inertia of the melancholic. We might see the healthy person's power of pursuing an end tenaciously exaggerated to the unshakeable delusion of the paranoiac. I need not give further examples, for I wish only to illustrate my point ; much more research will be necessary if these possibilities are to be explored thoroughly.

Cybernetics is not more than a few years old, and its application to psychology and psychiatry has hardly begun. Most of the workers who use cybernetics are applying it to communication engineering and to calculating machines; those who are applying it to the living brain are few. But they have the advantage that the field is new, almost completely unexplored, so that worth while discoveries are to be won fairly easily. For this reason I would like to take this opportunity of recommending the subject to those of you who are interested in research. Don't think that cybernetics demands a highly sophisticated technique ; Wiener's book, though magnificent in many ways, has given a most misleading suggestion in this respect. In fact, as a new branch of science, cybernetics starts almost from first principles, and what is needed for its application to the living brain is not so much an elaborate technique as a power of seeing the stale old psychological and physiological problems from a new angle.

I cannot claim this morning to have justified cybernetics to the psychiatrist, but I hope I have given sufficient evidence to show that cybernetics is a worthwhile study, and that further research in it offers excellent prospects. It is my belief that this new science will lead us steadily forwards, first to an increased understanding of how the brain works, and then to those therapeutic advances that we are all awaiting so impatiently.

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THE EFFECT OF SOME DRUGS ON THE ELECTRICAL ACTIVITY OF THE BRAIN, AND ON BEHAVIOUR.*

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Peripheral neuro-effector sites within and outside the autonomic nervous system form useful reference points for the study of the central effects of some agents. Nevertheless, ready analogies between peripheral neurohumoral mediation, and central synaptic transmission may be grossly misleading, and reliance must solely be placed on data derived from within the central nervous system itself.

A number of drugs known to have both peripheral and central actions (atropine, *d*- and *l*-hyoscyamine, physostigmine, di-*iso*-propyl-fluorophosphate, *dl*-, *d*- and *l*-amphetamine and *d*-lysergic acid diethylamide) were studied in terms of their effects on behaviour, and on the electrical activity of the brain in the experimental animal. Observations on some effects of *d*-lysergic acid diethylamide on normal volunteers, and of amytal, amphetamine, mephenesin, and *d*-lysergic acid diethylamide on catatonic stupor were also made.

Conscious, unrestrained cats, carrying multiple, permanently implanted cortical and stereotactically placed subcortical electrodes were used for the animal experiments. (1) Simultaneous observations on behaviour and electrical activity were made possible by the use of a constant environment chamber. Acute preparations subjected to high spinal or midbrain sections (the so-called *encéphale* and *cerveau isolé*) (2), and preparations anaesthetized with pentobarbitone, furnished complementary information.

In the conscious animal, large doses of atropine (2–3 mgm./kgm. i.p.) produced large-amplitude, slow waves, interspersed by bursts of fast activity. These patterns bore some resemblance to those characteristic of sleep. They did, however, differ from the latter in their failure to show a cortical alerting response to sensory stimuli, although the animals could, in fact, be roused. *l*-hyoscyamine induced effects similar to those seen with atropine; the dose, however, was lower (1–2 mgm./kgm. i.p.). *d*-Hyoscyamine was ineffective, even in high doses. Physostigmine (0·5–1·0 mgm./kgm. i.p.) abolished the slow activity induced by atropine and *l*-hyoscyamine, the resultant low-amplitude, fast activity resembling the normal alert pattern. Such activity was also produced by physostigmine alone. This activity, however, was not necessarily accompanied by a corresponding change in behaviour. Neostigmine left the electrical activity of the brain unaffected, even in doses which produced marked peripheral parasympathomimetic effects.

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d- and *l*-Amphetamine in full doses (3–5 mgm./kgm. by mouth) produced rhythms resembling those of the normal alert animal, i.e., low-amplitude, diffuse fast (15–30 cycles per second) activity in all regions. This was accompanied by a corresponding change in behaviour, the animal regularly becoming more attentive and excitable. The cortical response to rhythmic photic stimulation recorded over the visual area was increased in amplitude at all frequencies between 2 and 25 cycles per second. *d*-Lysergic acid diethylamide (15–25 microgm./kgm. by mouth) exerted effects somewhat similar to those of amphetamine on both electrical activity and behaviour. There was, however, no change in the response to photic stimulation.

In preparations anaesthetized with pentobarbitone (30 mgm./kgm. i.p.) the characteristic waxing and waning activity (the so-called barbitone "spindling") was changed by both physostigmine (0·5–1·0 mgm./kgm. i.v.) and D.F.P. (administered i.v. in divided doses up to a total of 3-4 mgm./kgm.); the spindle bursts were abolished, and replaced by continuous rhythmic activity at 4–6 cycles per second. Atropine sulphate abolished this continuous activity, and restored spindle bursts. Mid-brain section either reduced or abolished the D.F.P.-induced rhythmic activity, and restored an intermittent waxing and waning activity. Amphetamine had little effect on the electrical activity of a barbiturate anaesthetized animal as recorded at the cortical level. There was, however, some increase in the response to photic stimulation when recorded at the level of the lateral geniculate body. Large doses of *d*-lysergic acid diethylamide (50–100 microgm./kgm. i.p.) completely abolished the electrical activity characteristic of moderate barbiturate anaesthesia; the anaesthesia continued apparently unaffected.

The characteristic waxing and waning activity seen in the corticogram of the brain sectioned *in situ* at the level of the first cervical vertebra, or superior colliculus (2) was abolished by physostigmine and restored by atropine. In such experiments, simultaneous recordings of blood pressure and electrocortical activity showed the cortical activity to be unrelated to the transient changes in blood pressure produced by these drugs. The intermittent electrocortical activity of the *encéphale isolé* was abolished by amphetamine (in doses of 1·5–3·0 mgm./kgm. i.v.). This activity was, however, restored by section at mid-brain level in the same preparation, and remained unaffected by the administration of further doses of amphetamine. *d*-lysergic acid diethylamide (in doses of up to 100 microgm./kgm. i.p.) had no effect on the electrical activity of either of these acute preparations.

The effects of amphetamine and *d*-lysergic acid diethylamide on the corticogram thus differ from those of atropine, *l*-hyoscyamine and physostigmine in their apparent dependence upon mesencephalic or spinal connections. Again, there is better correlation between electrical activity and behaviour in the case of amphetamine and *d*-lysergic acid diethylamide, than there is with atropine, *l*-hyoscyamine and physostigmine. Magoun (3) has drawn attention to the existence in the upper brain stem of a reticular activating system, concerned with arousal by sensory stimuli. It is possible that amphetamine may act on receptors related to this arousal system. Amphetamine is structurally related to tyramine, *nor*-adrenaline, adrenaline, and not unrelated to mescaline. *d*-lysergic acid diethylamide is related to other adrenaline blocking agents of the ergot group. It is perhaps of interest that *nor*-adrenaline (4) and 5-hydroxytryptamine (5) have been recently identified in some areas of the brain, and that *d*-lysergic acid diethylamide has been found to antagonize 5-hydroxy-tryptamine (6). Possible effects of these drugs on the general and *local* cerebral circulation, and on intermediate metabolism (7) must, however, be very clearly borne in mind.

The symptoms of *d*-lysergic acid diethylamide (L.S.D.-25) intoxication were studied in 12 male and 3 female volunteers. The drug was administered in doses of 15 to 100 microgm. by mouth, and particular attention was paid to the effects of rhythmic photic stimulation (at 4 to 24 cycles per second) on the symptoms of intoxication. Subjective sensations, including the peculiar illusions of form, colour and movement experienced under these conditions, were sound recorded for each frequency, both before and after the administration of the drug. The sound-record was transcribed, and the transcript subsequently analysed independently for relevant elements. E.E.G. records were also taken.

The symptoms described by Stoll (8) were confirmed. Depersonalization, heightened awareness and fluctuating incongruous affect were the common symptoms. Visual symptoms were seen in 8 subjects, and 7 experienced distortion of body image. Mild dysarthria was seen in 11, and thought-blocking in 6 subjects. Rhythmic photic stimulation enhanced the symptoms in 12 out of 15 subjects ; in 3 out of these 12, symptoms were brought out where no symptoms of any kind had been experienced before. An uncommunicative, trance-like state during photic stimulation following L.S.D.-25 was experienced by six subjects ; and in three there was a slight, transient, but quite definite alteration in muscle tone, not unlike that seen in catatonia. This persisted for up to 20 minutes after photic stimulation had ceased. E.E.G. records were taken in 13 subjects. In terms of resting record, 2 of the subjects belonged to the micro-alpha, 5 to the responsive alpha, and 6 to the persistent alpha group (9) Following L.S.D.-25 the micro-alpha subjects showed little change in their resting record. One responsive subject showed micro-alpha activity, and four others became more responsive. Of the 6 persistent alpha subjects, 5 became completely responsive, and one remained persistent.

The effects of amytal (120–240 mgm. i.v.), amphetamine (7–15 mgm. i.v.), mephenesin (750–1,000 mgm., administered as a 5 per cent. solution in saline) and *d*-lysergic acid diethylamide (60–100 microgm. by mouth) were compared in 9 cases of catatonic stupor. The mental response was assessed in terms of verbal productivity and of drawing. The somatic changes recorded included blood pressure, pulse rate, foot temperature (recorded by multiple thermocouple), muscle tone (as measured in the flexors of the elbow by a simple weighting device) and sweat secretion. The well known effect of amytal on accessibility showed itself as an increase of both verbal productivity, and of drawing. There was better correlation between this change, and a rise in foot temperature, than between accessibility and muscle tone. An optimum mental response was only rarely accompanied by full muscular relaxation. Amphetamine decreased accessibility (10), a finding unlike its more common effects in normal subjects. Mephenesin regularly reduced muscle tone without changing either accessibility or foot temperature. L.S.D.-25 produced a response peculiar to itself, and unlike that seen either with amytal or amphetamine. This was characterized by unmotivated laughter and crying, bizzare uncontrolled behaviour, and an apparent activation of hallucinatory and delusional material. There was a blunting of the amytal response with repeated administration. Premedication with neostigmine (0·5 to 0·75 mgm. s.c.) or physostigmine (1·0 mgm., s.c.) did not modify the amytal response.

The above phenomena suggest the existence of elective affinities within the central nervous system. It is possible that chemical evolution has, at certain stages, accompanied phylogenetic evolution and, in the central nervous system, made use of selected variants of substances familiar to us as powerful neurohumoral transmitters at the periphery. There may be subtle and definite chemical differences between phylogenetically older and newer parts of the brain ; and even if such differences be confined to a few nodal points, a delicate shift in balance at these points could have profound effects on the function of the brain as a whole. Clear cut " levels" of action are perhaps less likely than changes in the temporal relation between the activities of unevenly distributed cell groups.

The above material was communicated to the Physiological Society at its meetings of January 16th (11, 12), and June 5th (13, 14), 1953.

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PSYCHOPHYSIOLOGICAL INVESTIGATIONS IN EXPERIMENTAL PSYCHOSES: RESULTS OF THE EXHIBITION OF D-LYSERGIC ACID DIETHYLAMIDE TO PSYCHIATRIC PATIENTS.

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d-Lysergic acid diethylamide (L.S.D.-25) was first prepared by Stoll and Hoffmann in 1938 (35) as a derivative of rye ergot. Its profound effects in minute doses were discovered accidentally by Hoffmann and reported by Stoll (34) along with additional observations by the latter on 16 healthy controls and six schizophrenic patients. With a dose of 30–130 γ (0·03–0·13 mgm.) Stoll (34) noted motor inco-ordination, disturbances of visual perception with illusions and hallucinations, clouding of consciousness, and affective changes principally in the direction of euphoria and distractibility. Subsequent clinical reports have confirmed these findings (6, 38). Becker (1) using doses of 30–40 γ in healthy controls attempted to predict the quality of the resulting psychosis from the constitutional somatotype of the subject; he contrasted maniacal hyperkinetic states with those showing inhibition and depersonalization and drew attention to the pattern of the visual perceptual disturbances, which were principally those of differences in size, clarity and perspective. Becker's attempts at somatotypological correlation were less successful than those of Condreau (4) who used mentally ill patients as well as healthy subjects and found that L.S.D.-25 did tend to reinforce pre-existing personality characteristics, especially with regard to mood changes. Rinkel and others (30, 7) with doses of 20–90 γ in mixed healthy and psychiatrically disturbed populations stressed the scotopic nature of the hallucinations and the greater frequency of illusions of rippling or wavy lines evolving at times into geometrical designs. Affective blunting with a lack of spontaneity was commoner than the production of major delusions. In epilepsy apparently visual hallucinations are more frequently concomitants of L.S.D.-25 administration than in other mental disorders (31).

Comparison of the effects of d-lysergic acid diethylamide with other agents producing experimental psychoses has been made (9, 39, 13, 38). With doses of 10–120 γ L.S.D.-25 and 0·4–0·6 gm. mescaline in schizophrenics (13), similar qualitative effects were found with both drugs although the changes were considered quantitatively greater with mescaline. Fischer and others (9) reported essentially similar findings using doses of 130 γ L.S.D.-25 and 0·5 gm. mescaline, but suggested that the new drug evoked a clinical picture resembling much of the phenomenology of hebephrenia while the mental state in mescaline intoxication was more akin to that of paranoid schizophrenia with catatonia.

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Aside from such clinical descriptive studies, some physiological work has been carried out. A pilot study of six schizophrenic patients using ascending doses of 0·5–6·0 γ per kg. body weight (10) showed a leucocytosis but no constant change in the E.E.G., E.K.G., blood N.P.N., liver function tests or urine. Arterial blood pressure and pulse rate tended to be slightly raised and the blood sugar showed a slight elevation of 5–6 mgm. per 100 c.c. Respiration was apparently unaffected but salivation and lacrimation increased and the pupils frequently showed dilatation. A similar lack of response of the blood N.P.N. and the blood sugar, and of the arterial blood pressure and body temperature was noted by Busch and Johnson (2). Rinkel and others (30) observed a tendency towards an increase in the alpha frequency of the E.E.G. by some 1–3 c./sec. Fischer and others (9) found a normal response to the hippuric acid excretion test for L.S.D.-25 as opposed to evidence for impaired liver function after mescaline intoxication using Quick's test. The cinnamic acid test, however, yielded abnormal results for L.S.D.-25 in their hands.

Investigation of the carbohydrate metabolism (25) indicates that L.S.D.-25 administration is followed by an increase in blood glucose and hexosemonophosphate but no change in lactate or pyruvate levels. An increase in glycogen metabolism together with a block in the breakdown of hexosemonophosphate is therefore a possible mechanism of action of L.S.D.-25.

Psychological studies of the lysergic acid psychosis have been made by Stoll (34), de Shon and co-workers (7) and by Matefi (24). Characteristically schizophreniform Rorschach responses were obtained with evidence on other tests of impaired emotional inhibition and tangentiality of thought.

The present psychophysiological investigation was designed in the hope that some of the clinical findings reported in the literature might yield to objective methods of study. In the sense that the deliberate production of an iatrogenic psychosis represents a model experiment, new knowledge of the mechanisms of action of idiopathic psychotic states may follow upon such investigations.

EXPERIMENTAL PROCEDURES.

Clinical Material.

A total of 33 subjects were studied. Of these 14 were healthy controls of a mean age of 28 and an age range of 20–40 years. There was an equal number of males and females. All were volunteers (with the obvious bias of such selection) and all were psychiatrically sophisticated since they represented medical psychiatric colleagues and members of the nursing, occupational therapy and research departments of the Hospital.

The remaining 19 subjects were psychiatric in-patients of the Maudsley Hospital. They comprised seven male schizophrenics with a mean age of 28 and a range of 20–32 years. This group included four paranoid schizophrenics, one catatonic, one case of hebephrenia and one of dementia praecox simplex.

The remaining 12 patients suffered from affective disorder—depression. There were nine males and three females and the age range was 23–56, with a mean age of 41 years. The diagnoses in this group ranged from those with comparatively mild reactive depressions through one example of a severe endogenous depression and another complicated by obsessive compulsive complaints up to two patients in whom severe symptoms were linked with delusions and suicidal pre-occupation. Anxiety was not a marked finding in any of the group, all of whose primary symptoms of depression had been sufficiently impelling to demand admission to hospital.

Method.

d-lysergic acid diethylamide was given by mouth to the fasting subject in the form of the freshly prepared tartrate, and in a dose of 40 γ. Additional higher doses up to 120 γ were given to a selected few of the patients, but not to any of the controls. In the case of three of the controls a placebo was administered under identical conditions to those in which the drug was employed.

The subjects were investigated at intervals throughout the period of maximum action of the L.S.D.-25 (i.e., 2–4 hours after its exhibition) and during this time the results of a formal mental-state examination were recorded. A comparable control period of observation was arranged for each subject either one week before or one week after the day on which the drug was given. The subjects were randomized for this purpose and it was hoped that such a procedure might minimize the effect of practice on the scores.

In addition to the mental-state examination, behavioural change was recorded on a modified Maudsley Hospital Behaviour Chart and scored under the headings of speech and thought, motor activity and general behaviour. Mood was rated separately on a five-point scale. Objective and subjective judgments were recorded separately.

A routine neurological examination was made and estimates of the pulse rate, arterial blood pressure and body temperature were made regularly throughout the period of observation.

Psychological Investigations.

Attention and concentration were tested by a battery consisting of the timed "serial sevens," digit retention [from the Wechsler-Bellevue Scale (37)] and a modification of Wittenborn's (40) remembered numbers test. *Memory* was assessed by the Wechsler Memory Scales and by the recall of a name, address and message after a period of five minutes. *Fluency, imagery and emotional lability* were estimated from the responses to cards I, II, IV and X of the Rorschach and Behn-Rorschach series given in two parallel sets, randomization of the subjects being carried out to determine which set should be used first. *Speed of oscillation* (11, 3) was measured in terms of the number of reversals noted passively in a four-inch square Necker cube during a 30-second period of observation. Active and inhibited scores were also determined by instructing the subject to attempt maximally to speed the reversed rate and then similarly to slow it. *Eidetic imagery* tests (14) were employed to elicit the total duration of the stimulus after-image under controlled conditions, the time during which the after-image has well-defined outlines, the differentiation between the eidetic- and after-image by Emmert's law, the density of the after-image, and "latent" eidetic phenomena. Since perceptual anomalies brook large in the clinical descriptions of the L.S.D.-25 psychosis, all subjects were additionally requested to report their visual sensation both with their eyes closed and later whilst pressure was applied to the globes. A number were taken into a darkened room and a few had music played over to them in an (unsuccessful) attempt to produce synaesthesiae. Assessments of *duration of the passage of time* were made by the subjects following the instruction to estimate four separate periods of 15 seconds; their scores were taken as the mean of these estimates. *Motor efficiency and time duration* were assessed by Kraepelin's test in which the subject is asked to tap with the point of a pencil as quickly as possible on one side of a piece of quarto paper. The test is interrupted at the end of 15 seconds and is then repeated using the other hand on a fresh sheet of paper for a similar period. The score is recorded as the combined total of taps for each hand. At the conclusion of each period of tapping the subject was asked to estimate the length of time he had been tapping the paper.

Physiological Observations.

Spectroscopic oximetry.—The "reduction time" (36, 27) of the arterialized capillary blood in vessels of the skin of the finger nail fold was estimated by a method already described by one of us in detail elsewhere (19). Results are expressed as R.T. secs. and are capable of conversion into equivalent arterial oxygen saturation percentages (18). Combination of the resting levels with the results of such oximetric measurements understand ardized apnoeic stress results in the calculation of an R.T. "efficiency score" (28) and a knowledge of these two dimensions of the oximetric response represents an objective technique for determination of psychiatric diagnosis (19), evaluation of the emotional state (20) and of assessing differential perceptual response patterns (21, 33). Resting levels and efficiency scores were measured in all subjects of the investigation and the results with and without the drug compared. In addition, oximetric determinations were combined with other psychophysiological procedures (*vide inf.*).

Cardiovascular response to stress.—The Hines-Brown (12) cold pressor test was modified to extend the time of immersion of the hand to three minutes, since pain seems to be the evocative stimulus in this test (42) and it has been shown that pain is maximal within such a three-minute period (41). Arterial blood pressures were estimated sphygmomanometrically as frequently as possible during the time of the test and continued until three consecutive readings at the pre-test level were recorded, or until ten minutes had elapsed after removal of the hand from the ice-water. In several experiments these blood pressure recordings were combined with concurrent spectroscopic oximetric estimations, readings being similarly continued until pre-test conditions had again been attained.

Oxygen consumption and spirometry.—A Benedict-Roth metabolism apparatus was employed to measure the resting metabolic rate and oxygen consumption per minute. Recordings were taken with the subject in a fasting condition and after he had been lying down comfortably for 30 minutes. The tracings were analysed also to determine the respiratory rate and pattern after the method of Finesinger (8) which involves the summation of seven readily determined variables into a numerical score.

The Controlled Stress Test (C.S.T.).—This procedure designed (22) from C. G. Jung's (15) discrete word association test and Rapaport's (26) more recent modification of it, consists of the presentation of parallel series of 15 potentially traumatic and neutral words, Rorschach cards and T.A.T. pictures as stimuli to the subject, oximetric determinations being made and reaction times taken at the moment of the subject's response.

Statistical Analysis.

In view of the relatively small number of subjects employed in this investigation, the u test of Lord (16) was computed for purposes of evaluation of the results. This statistical procedure is based on range estimates of standard deviation of the t test.* The use of range estimates sacrifices some of the efficiency of root mean square estimates, but the work of Davies and Pearson (5) suggests that information is not discarded to any serious extent, provided that the number of observations in the sub-samples is not greatly in excess of ten.

RESULTS.

Clinical State.

The findings here are summarized in Table I. They may conveniently be grouped under the following headings :—

Physical signs.—The only frequent physical signs noted were flushing of the face, enlargement of the pupils without impairment of the light or convergence reactions, and unsteadiness of gait and co-ordination which, whilst a frequent subjective complaint, was minimal and never amounted to clinical ataxia. Temperature and blood pressure showed slight and inconstant changes. Complaints of nausea or dry mouth with sensations of chilliness alternating with hot flushing were also common. These physical findings occurred with equal frequency in all groups.

Mental state.—Overt behaviour showed little change in any of the groups, although of the controls four were rated as overactive compared to only one before, and three as underactive. However, many of the subjects, if unstimulated by questions and testing, tended to sit quietly in a soporific manner, but this was never of a sufficient degree to be regarded as withdrawal. Speech was unchanged in both groups of patients and equally increased or decreased in the controls. Mood proved to be a significant variable. The outstanding

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* Lord's u is given by $\frac{\Sigma D}{NR}$ where the numerator is the summation of the individual differences and the denominator represents the number of individuals in the group expressed as a multiple of the extent of range deviation summed algebraically.

TABLE I.—*Differential Incidence of Clinical Changes Evoked by L.S.D.-25 Administration in Healthy Controls and Patients with Two Types of Psychiatric Disorder.*

		Healthy controls (10)		Schizophrenics. (6)		Depressives. (12)		Totals. (28)	
		Control period.	L.S.D.-25.	Control period.	L.S.D.-25.	Control period.	L.S.D.-25.	Control period.	L.S.D.-25.
Speech and thought	Deluded	0	0	4	4	2	2	6	6
	Speaks little	1	4	2	2	7	8	10	14
	Speaks much	2	4	1	1	0	0	3	5
	Perplexed	0	0	0	0	0	3	0	3
Activity and behaviour	Foolish giggling	0	5	1	3	0	1	1	9
	Withdrawn and preoccupied	1	3	3	4	6	6	10	13
	Overactive	1	3	1	1	0	0	1	4
	Underactive	1	4	2	3	6	7	9	14
Mood	Suspicious	0	2	0	0	1	1	1	3
	Rapid mood change	1	4	0	0	0	0	1	4
	Depressed	0	2	1	2	12	8	13	12
	Overcheerful	0	6	0	3	0	1	0	10
	Less depressed	0	0	0	0	0	3	0	3
	Anxiety	0	1	1	0	1	3	2	4
Physical	Flushing	0	3	0	3	0	6	0	12
	Enlarged pupils	0	6	0	4	0	9	0	19
	Unsteadiness	0	1	0	0	0	3	0	4
Subjective	Nausea	0	3	0	0	0	1	0	4
	Dry mouth	0	3	0	0	0	4	0	7
	Hot/chilly	0	2	0	1	0	1	0	4
	Unsteadiness	0	6	0	3	0	1	0	12
	Sleepy	0	3	0	3	0	1	0	7
	Forced laughter	0	5	0	2	0	0	0	7
	Time slowed	0	2	0	0	0	1	0	3
	Well being	1	6	0	3	0	1	0	10
	Visual illusion	0	4	0	0	0	0	0	4
	Lack of concentration	0	4	1	2	0	1	1	7
	Apprehension	0	2	0	0	0	5	0	7

effect in both controls and schizophrenics was a euphoriant one, combined with a subjective feeling of well being and episodic foolish and rather forced laughter. However, in the group of depressives this reaction was only shown in one patient, although three others showed some slight lightening of mood. Contrasting with these, two of the controls showed slight depression. Where anxiety and tension were originally present they were heightened and in no case diminished. Where delusions were present they remained unchanged but no fresh ones were produced. Increased suspiciousness was shown by a few subjects both amongst patients and controls, but this never extended to persecutory ideas. Where aural hallucinations were present these were also unchanged, but neither fresh aural nor visual ones were produced. Four of the controls complained of unformed visual illusions usually consisting of flickering lights with an heightened perception both for intensity of illumination and colour. In no case were such visual changes impressive. In all cases there was complete retention of insight, any effects produced being attributed to the drug by both patients and controls.

The Effect of a Placebo.

The changes manifested by the three members of the control group to whom this was given appeared to be directly related to their degree of "clinical sophistication." Thus the first produced complaints of depression, lability, which he likened to alcoholic intoxication, restriction of the lateral fields of vision, slight deafness, dulling of smell, feelings of pressure and fever, loss of libido and of sense of time combined with difficulty in thinking and of finding correct words. The second, with less knowledge, merely complained of a sense of intoxication with difficulty in concentration and the finding of words, whereas the third, with little knowledge of the expected reaction, noticed no untoward changes. The test scores of these three, however, were not significantly altered in any measures.

Psychological State.

Attention and concentration.—The mean time for performing the serial sevens test was increased in all groups without however appreciable impairment of accuracy. Statistical analysis showed these increases to be significant at the 5 per cent. level of confidence for both the normals and the schizophrenics. In the concentration test there was a slight increase of score in the normals with a decrease in the schizophrenics and depressives, but these changes were not significant. Table II gives the data on these two tests.

TABLE II.—*Effect of L.S.D.-25 on Attention and Concentration.*

			Mean scores.				
Test.	Group.	N.	Control period.	L.S.D.-25.	Difference.	"*u*"	P.
Serial sevens (time in seconds)	Controls	10	29·9	34·7	+4·8	0·23	5%
	Schizophrenics	5	47	57	+10	0·68	2%
	Depressives	8	60	65	+5	0·11	N.S.
Serial sevens (errors)	Controls	10	0·2	0·2	0	—	—
	Schizophrenics	5	1	1·6	+0·6	0·6	2%
	Depressives	8	1	−0·36	−0·36	0·04	N.S.
Concentration	Controls	10	54·2	58·7	+4·5	0·08	N.S.
	Schizophrenics	5	50·6	43·8	−6·8	0·42	N.S.
	Depressives	10	43·6	38·3	+5·3	0·12	N.S.

Memory.—The effect of the drug on visual memory scores was to show a slight and insignificant decrease in all groups which was maximal in that of the depressives. There was no significant decrease in the accuracy of recall of a message, although such a response tends to be global and unsuited for the detection of small changes of memory. Digit retention showed no significant change in any group. Table III lists the data on these tests.

TABLE III.—*Effect of L.S.D.-25 on Memory.*

			Mean scores.		
Test.	Group.	N.	Control period.	L.S.D.-25.	Difference.
Visual memory	Controls	10	13·8	13	−0·8
	Schizophrenics	5	12·6	11·2	−1·4
	Depressives	10	9	5·8	−3·2
Digit retention	Controls	10	14·4	14·1	−0·3
	Schizophrenics	5	11·2	11	−0·2
	Depressives	10	10·7	10	−0·7
Errors of recall	Controls	10	0·3	0·3	0
	Schizophrenics	5	0·2	0·2	+0·2
	Depressives	10	0·25	0·6	+0·37

Time.—Estimation of duration showed a slight but insignificant mean reduction in normals and in depressives, i.e., time appeared to pass more quickly (Table IV).

TABLE IV.—*Effect of L.S.D.-25 on Apparent Duration.*

Group.	N.	Mean scores (seconds). Control period.	L.S.D.-25.	Difference.
Controls	5	13·4	11·2	−2·2
Depressives	8	8·4	7·7	−0·7

Oscillation.—There was no significant difference in rate or in ability to change the frequency of reversal in either the controls or depressives on whom the test was performed. The subjects used were too few to make any valid correlations with mood change (Table V).

TABLE V.—*Effect of L.S.D.-25 on Rate of Reversal of Necker's Cube.*

Test.	Group.	N.	Mean scores—Reversals/min. Control period.	L.S.D.-25.	Difference.
Passive	Controls	3	11	9·4	−1·6
	Depressives	7	9	8·2	−0·8
Active	Controls	3	22	18·6	−3·4
	Depressives	7	11·4	11·4	0
Inhibited	Controls	3	8	5·4	−2·6
	Depressives	7	6·4	6·4	0

Rorschach.—Measurements of the total number of responses, the number of human responses and the sum of the weighted colour responses were undertaken.

In the control group, five subjects showed an increase in their number of responses under lysergic acid and five a decrease. This change did not appear dependent on whether the control record followed or preceded the one under the drug. It should be noted that, in all cases except one, the subjects showed fewer responses on the Behn cards than on the Rorschach ones. The number of human responses decreased in three cases, remained the same in five and increased in two. The sum of weighted colour decreased in three cases, remained the same in two and increased in five. Four of the six subjects who were clinically rated as overcheerful gave this increased response. A qualitative comparison of the records again showed no marked trends of change: two of the subjects gave much poorer records in terms of fantasy and two brought up many more sex responses.

Of the eight members of the depressive group who completed the test, only one showed an increase of the total number of responses, whereas four showed a decrease. None increased in the number of movement responses, whereas three decreased. The sum of the weighted colour increased in three cases, decreased in one and was the same in the other four. These three who increased included the patient who was clinically rated as overcheerful and one of the two who were considered to be less depressed under the drug. However, of the four patients who refused one or more cards on the control day, only one refused a card when under the drug and even she one card only, whereas before she had refused two. This might indicate some greater degree of participation or interest in the task.

In the six schizophrenics the changes were random and inconsistent and there was no relationship between weighted colour responses and mood.

Controlled Stress Test : Reaction times.—In the normals the mean speed of response to stimuli which were considered non-traumatic showed no consistent trend, and this was also the case in the depressive and schizophrenic group. The difference between the speed of response to traumatic and to non-traumatic stimuli was also insignificantly and inconsistently changed. Oximetric results will be considered below.

Eidetic imagery.—No subject showed eidetic imagery as judged by Jaensch's (14) criteria. The mean time of duration of the after-image showed a trend towards an increase in all groups, but this was not statistically significant. The size of the after-image conformed closely to Emmert's law both under control conditions and under the drug and again there was no significant change in the measurement (Table VI).

TABLE VI.—*Influence of L.S.D.-25 on Eidetic Variables.*

			Mean scores.		
	Group.	N.	Control period.	L.S.D.-25.	Difference.
Duration of A.I. in seconds	Control	6	34·4	43·5	+9·1
	Schizophrenics	3	35·2	38·2	+3·0
	Depressives	9	29·0	29·9	+0·9
Mean size of A.I. at 25 cm. in cm.	Controls	6	6·6	6·9	+0·3
	Schizophrenics	3	6·5	6·5	0
	Depressives	8	6·2	6·2	0

Physiological State.

Arterial blood pressure : (a) *Systolic.*—The mean resting levels of both the depressives and schizophrenics were significantly higher than the healthy normals and there was a correspondingly greater maximal and mean rise following the pain stimulus, although this was in fact relatively smaller than in the controls. However these measures, with in addition, the mean level of fall (from five minutes to the cessation of recording), the time to return to resting levels and pulse pressure, all showed no significant variation under the drug.

(b) *Diastolic.*—The resting diastolic levels were again higher in the depressives and schizophrenics with corresponding higher mean and maximal rises after stimulation than in the controls. The relative rise (between resting level and the maximal and mean heights) was greatest, however, in the schizophrenics and least in the depressives. Again all these means with, in addition, the mean of the level of fall and the time required to return to resting level showed no significant difference under the drug.

It was interesting to note, in confirmation of the work of Malmo and Shagass (23), that the schizophrenic patients showed a normal reactivity to stress although, of course, none of these subjects was deteriorated. The detailed results are given in Table VII.

TABLE VII.—*Effects of L.S.D.-25 on the Arterial Blood Pressure in the Modified (Three Minute) Cold Pressor Test.*

			Systolic.			Diastolic.		
			Mean scores (mm. Hg.).			Mean scores (mm. Hg.).		
Measure.	Group.	N.	Control period.	L.S.D.-25.	Difference.	Control period.	L.S.D.-25.	Difference.
Resting level	Controls	10	117	116	−1	72	74	+2
	Schizophrenics	5	134	127	−7	77	76	−1
	Depressives	8	128	134	+6	81	82	+1
Maximal rise	Controls	10	148·2	143·1	5·1	101	101·4	+0·4
	Schizophrenics	5	160·8	159·6	−1	112	116·4	+4·4
	Depressives	8	153·7	160	+6·3	100·2	102·7	+2·5
Mean rise	Controls	10	136	133	−3	91	94	+3
	Schizophrenics	5	149	147	−2	100	105	+5
	Depressives	8	141	133	−8	92	92	0
Difference—Resting level and mean rise	Controls	10	18·1	15·8	−2·3	18·8	19·7	+0·8
	Schizophrenics	5	12·4	18	+5·6	23·4	26·8	+3·4
	Depressives	8	13·8	12·9	−0·9	12·7	11	−1·7
Difference—Resting level and maximal rise	Controls	10	31·2	27·1	−4·1	29	27·4	−1·6
	Schizophrenics	5	26·8	32·6	−5·8	35	40·4	+5·4
	Depressives	8	25·7	26	−0·3	19·2	20·7	+1·5
Level of fall 5 minutes	Controls	10	117	120	+3	77	79	+2
	Schizophrenics	5	126	128	+2	76	81	+5
	Depressives	8	130	139	+9	81	84	+3
Time to fall (minutes)	Controls	10	7	7	0	7	7	0
	Schizophrenics	5	5	6	+1	6	6	0
	Depressives	8	5·7	5·7	0	5·7	5·5	−0·2
Pulse pressure	Controls	10	44·3	41·9	−2·4	—	—	—
	Schizophrenics	5	56·4	51·2	+5·2	—	—	—
	Depressives	8	45·1	50·7	+5·6	—	—	—

Spectroscopic Oximetry : (a) *Resting oximetric status.*—The effect of L.S.D.-25 on this variable was to raise the reduction time values in the healthy and depressed groups of subjects and to leave the schizophrenic patients unchanged. Lord's test showed these results to possess statistical significance ($u = \cdot 25$; $p < \cdot 05$ for healthy normals. $u = \cdot 23$; $p < \cdot 05$ for the depressed patients. $u = \cdot 08$; p is N.S. for the schizophrenics). A similar pattern of change was also observed after computation of the "efficiency score," marked rises occurring in the patients with affective disorders, lesser rises in the healthy group and no change in the schizophrenics. Table VIII gives the actual figures obtained.

TABLE VIII.—*Effect of L.S.D.-25 on Oximetric Status. The Efficiency Score is Given by* $\frac{(\text{R.T.}) - (\text{R.T. } \textit{with Apnoea})}{(\text{R.T.})} \times 100$ *and may therefore Result in Negative as well as Positive Quantities.*

		Mean resting oximetric status.					Mean efficiency scores.				
Group.	N.	Control period. R.T. (secs.).	L.S.D.-25. (R.T. (secs.)	Difference. (secs.).	*u*.	P.	Control period.	L.S.D.-25.	Difference.	*u*.	P.
Controls	11	45·54	59·92	+14·38	0·25	0·05	+26·7	+32·4	+5·7	0·14	N.S.
Schizophrenia	7	35·00	35·60	+0·60	0·08	N.S.	+26·0	+25·0	−1·0	0·13	N.S.
Depressives	12	36·57	50·92	+14·35	0·23	0·05	+6·6	+31·6	+25·0	0·43	0·001

(b) *Oximetric monitoring of the Cold Pressor Test.*—Oximetric estimations were made simultaneously with the recordings of the blood pressure. As may be seen from Table IX, the usual result of the application of cold water stress is to produce a marked fall in the R.T. (sec.) values. Under the influence of L.S.D.-25 the extent of this fall was increased ($u = \cdot 56$; $p = \cdot 01$ for depressed patients), and similarly the duration of the fall is prolonged before pre-stress levels are again attained ($u = \cdot 37$; $p = \cdot 02$ for depressed patients).

TABLE IX. *Effect of L.S.D.-25 on the Oximetric Response to the Standardized Pain Stress Provided by a 3-minute Modification of the Hines-Brown Cold Pressor Test.*

		Oximetry before lysergic acid.		Oximetry 4 hours after 40 gamma lysergic acid.	
Group.	N.	R.T. secs.	" Efficiency score."	R.T. secs.	" Efficiency score."
Controls	11	45·538	+26·69	59·923	+32·38
Schizophrenics	7	35·000	+26·00	35·600	+25·00
Depressives	12	36·570	+ 6·64	50·923	+31·62
Totals and Means	30	39·969	+17·81	50·625	+31·156

(c) *Oximetric monitoring of the Controlled Stress Test.*—The spectroscopic oximetric responses to the potentially non-traumatic (N.T.) and to the potentially stressful (T.) stimuli were pooled for each diagnostic group both for the untreated and drug-influenced conditions. Lord's test showed that, for the healthy controls, a significant rise occurred in the (N.T.) responses ($u = \cdot 26$; $p = \cdot 05$) and in the (T.) responses ($u = \cdot 27$; $p = \cdot 02$). The rise was not however significant for either (N.T.) or (T.) in the depressive or schizophrenic patients.

An estimate of total reactivity in terms of the emotionally conditioned psychological stimuli in the C.S.T. is given by the individual differences. [(N.T.) — (T.)] between the two types of stimuli. These estimates were computed for each diagnostic group and evaluated statistically. Increased reactivity resulting from the exhibition of the drug was found in the controls ($u = \cdot 21$; $p = \cdot 05$) but no such increase occurred in the case of the psychiatric patients.

Comment.—It is of interest that the results of determining the resting oximetric status of the present healthy control group are in accordance with those obtained in a previous investigation (19) in which an entirely different, military control population was sampled. In that latter research it was shown that such a healthy group was capable of differentiation from a variety of mentally-ill groups on the basis of a combination of the resting oximetric status and the efficiency score. Apposite to our present purpose is the distinction found for the " organic neurological " group of patients for these showed abnormally high resting R.T. values, their range corresponding almost exactly to the raised values found in subjects intoxicated by L.S.D.-25. This is presumptive evidence of the organic nature of the psychosis provoked by this drug.

Of equal relevance is the behaviour of the efficiency score which has been found to provide a delicate means of differentiating as well between healthy groups with regard to their physical status (29) as between health and organic disease (28) and as between health and mental disturbance (17, 19). In the latter connection, it was found that efficiency scores below + 5 were associated with psychoneurotic reaction patterns (19). The effect of L.S.D.-25 on the depressed patients in the present investigation was to cause a marked and highly significant ($p = \cdot 001$) increase from a mean of + 6·7 to a mean of + 33·4. By contrast, the healthy control subjects, who could be regarded by the criterion as physiologically efficient, showed merely an insignificant trend from a mean of + 26·63 to one of + 31·54.

The interpretation of these findings is complicated by the heterogeneity of the depressive group, including as it did patients of differing categories, who have been found in the past to yield quite distinct oximetric readings. However, as a group, they may be said to have reacted homogeneously in this respect, although the lowest rises of R.T. score were found in the endogenously depressed patients, and conversely the highest in those whose illness was predominantly reactive. These highest rises did in fact occur in those whose very low resting scores (all zero or below), in addition to the clinical evidence, placed them in the neurotic group. In four of the six these increases could be correlated with both subjective and objective lightening of mood.

Thus, if the R.T. score be regarded as a valid measure of improved physiological efficiency, this change could be equated with an improved affective state. However, it must be added that the smallness of both the numbers of the subjects and the clinical changes manifested prohibited more than inference being drawn.

In the schizophrenics, however, there was merely a non-significant trend toward a reduction of R.T., both resting and under the stress of breath holding. The R.T. scores showed a mean increase of 9·5 which was not significant.

Thus the schizophrenics could be regarded as showing a diminished or unchanged autonomic reactivity under the drug, although it should be kept in mind that their levels, although lower than those of the present group of controls, lay within previous control limits (19).

The influence of the vasodilatation, showed by the majority of the subjects on this test, remains undetermined, and it is hoped to investigate this point further. However, for the purposes of this study, namely objective differentiating measures, the findings would appear to remain valid.

Kraepelin's Tapping Test.—Only random changes were noted in all groups when the results under the drug were compared with those of the control period.

Pulmonary function and oxygen consumption.—Spirograms could only be run in eight of the controls and three of the schizophrenics, and the smallness of the latter group hampered comparison.

However, the schizophrenics, although showing a mean resting oxygen consumption of 18·5 c.c. per minute more than the controls, increased this by a further mean of 18·3 c.c., which was just below the 5 per cent. confidence level. This was associated with a mean increase of respiratory rate of 3·3 respirations per minute and of total score of 1·3, neither of which were significant. By contrast, the controls showed random changes only in oxygen consumption, but a raised respiratory rate of 2 per minute, which was significant at the ·001 level of confidence.

In addition the total score showed a tendency towards an increase (mean = 3·4), which was not significant. Of the subscores, that recording "major fluctuations" showed the greatest mean increase of 2·1, but this was also not significant.

Thus in both groups there was an increased irregularity of respiratory pattern, and quickening of respiratory rate, with, in the schizophrenics, an increased oxygen consumption.

Discussion.

The clinical changes resulting from a dosage of 40 γ of d-lysergic acid diethylamide were not gross, although euphoria, when present, was unmistakable.

Only incidental observations were made of the effect of larger amounts of the drug, which were not given to the controls. Doubling or trebling the dose to 80 γ and 120 γ did not produce significantly different results in the few subjects in whom it was tried, but these were mostly the schizophrenic patients who had been noted to be resistant to its effects. In one member of the depressive group, however, a mood slightly lightened by 40 γ became despondent and suicidal on 80 γ.

In general, mood changes seemed dependent upon the original affective state of the subject, equanimity and cheerfulness tending toward euphoria, whereas anxiety and depression were usually heightened. There was some suggestion, however, of a possible differential response between those patients with endogenous and those with reactive depression in that there was a higher proportion of the latter who showed some improvement of mood, but this may merely have been a product of the differing severity of the two groups of illness. Certainly in the present state of knowledge, the drug would seem of little therapeutic value in depressive states.

The absence of significant changes in concentration and memory contrasted with the subjective impressions of distractibility and intoxication, although the influence of what we have termed "clinical sophistication" in the controls, and suggestion in the other groups on subjective estimates, remains a variable factor in such investigations.

The Rorschach test would seem unsuitable in the assessment of minor changes of mood and outlook where the "historical perspective" of the individual is basically unchanged.

Perceptual changes were certainly not notable and the illusions manifested were minimal in degree. Thus paucity of clinical change was merely confirmed by the test of eidetic imagery, but it would be instructive to repeat this with larger, hallucinatory doses. It should, however, be noted that a recent study by Saltzman and Machover (32) failed to show eidetic imagery by a similar experimental procedure in hallucinating alcoholics.

In general, it appeared that slight, although clinically apparent, changes produced by the drug were difficult to verify objectively. At present many of our distinguishing tests, both physical and mental, are too crude and new measures are required. Illustrative of this was the apparent increased discriminatory power of oximetry, an estimate of capillary change, when compared to oscillomentry, dependent upon arterial change.

Similarly a study of respiratory function, closely linked as it is as well with speech as with bodily homeostasis, would appear profitable and, although for the present comparative purposes the Benedict Roth machine proved adequate, a more sensitive and less restrictive apparatus might prove more rewarding. It seems important, however, to measure oxygen consumption in addition to respiratory excursions.

Thus future investigation, in producing further refinements of such functional tests, may not only yield profiles of psychophysiological pattern serving to amplify and extend clinical description, but also lead to an increased understanding of bodily mechanisms in mental disease.

Summary.

(1) d-lysergic acid diethylamide (L.S.D.-25) was given to 11 healthy controls, 12 patients with predominant depression and 7 patients with schizophrenia, in an attempt to obtain comparative objective estimates of some of the psychological and physiological changes produced. 40 γ of the tartrate was given orally and a few incidental observations made of the effects of larger doses up to 120 γ.

(2) Clinically the changes resembled those previously described and were not gross. Accentuation of pre-existing affect was commonest, with associated lability of mood, and retention of insight.

(3) There was no measurable impairment of memory and concentration.

(4) Perceptual changes were uncommon and confined to unformed visual illusions in four of the controls. Tests of eidetic imagery showed no eidetic tendency under the drug.

(5) Reversal of perspective in an ambiguous figure was unchanged in the depressives.

(6) Qualitative and quantitative estimations of the Rorschach showed no significant change.

(7) An increased uptake of oxygen in the three schizophrenics who had spirograms taken while under the drug contrasted with only random changes in the controls. Both groups showed an increased respiratory rate.

(8) The response of the blood pressure to a pain stress showed no significant variation or differential response between the groups.

(9) Spectroscopic oximetry carried out during this pain test and in the "controlled stress" of a word association test showed significant changes however, which were interpreted as indicative of increased autonomic lability in the controls and depressives as contrasted with unmodified functioning in the schizophrenics. It seemed that oximetry had detected a change not apparent in the grosser measures of oscillometry.

(10) Similarly resting oximetric readings showed a differential response pattern between the schizophrenics, the controls and the depressives.

The efficiency score was very significantly raised in the depressive group, the greatest change being manifested in those whose illness was predominantly reactive. If this finding be regarded as indicative of improved physiological functioning, it could be correlated in four of the six patients with some alleviation of their depression.

(11) In conclusion, it proved difficult to obtain valid differentiating measures of clinically apparent changes.

The difficulty was felt to lie in the paucity of tests which were sufficiently discriminative, and it was considered that an elaboration of sensitive physiological recordings would facilitate the study of experimental intoxications in particular and of mental disease in general.

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BENZOIC ACID DETOXICATION IN SCHIZOPHRENIC PATIENTS.

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Quick (1931) first reported on the conjugation of benzoic acid in man and recorded the hippuric acid excretion rate as a test for liver function. Quastel and Wales (1938) found faulty detoxication in catatonic schizophrenic patients and later (1940) a return to normal values after clinical remission. A number of other workers, particularly Georgi, Fischer, Weber and Weiss (1948–49) described this disturbed benzoic acid detoxication as a general syndrome in all schizophrenics. When giving glycine simultaneously with the benzoic acid they noticed a normalized and increased hippuric acid excretion rate in patients who originally showed decreased hippuric acid excretion. The Quick test, modified in this way, was used in order to prove that the decreased hippuric acid excretion rate is not the expression of a disturbance in the coupling mechanism between benzoic acid and glycine but rather a disturbed ability of the organism to mobilize glycine. Mall and Jünemann (1952) have lately confirmed the results of Georgi *et al.* in extensive investigations. They reached the conclusion that variations in the hippuric acid excretion rate are mainly due to a disturbance of the ability to dispose of glycine in the schizophrenic organism. They confirmed previous results of Georgi according to whom treatment of the patients, which was carried out partly from the point of view of disturbed liver function only, partly combined with insulin and electroshock, leads to improvement of the detoxication rate. Persky, Gamm, and Grinker (1952) have also recently seen decreased hippuric acid excretion values in catatonic schizophrenic subjects, and have reported a return of the hippuric acid excretion to normal after successful psychiatric treatment. In their series patients who manifested free anxiety symptoms, excreted elevated amounts of hippuric acid ; the excretion rate returning to normal levels after successful psychiatric treatment.

The present authors have carried out investigations using the original Quick test and its modification described by Georgi, in a series of schizophrenic patients, and made some observations concerning an apparent connection between adrenal cortex function and the hippuric acid execretion rate. The results seem to be worth reporting.

Experimental.

The investigations were carried out on eleven acute male schizophrenics, with a disease duration under one year, and 54 chronic male schizophrenics with a disease duration of between 2–16 years. The nutritional state of all the patients was satisfactory, tuberculosis could be excluded in each of them and they were all under good general care.

In carrying out the Quick test we closely followed the technique described by Mall and Jünemann (1952); one of us (B. G.) having repeatedly carried out the tests before in Professor Mall's laboratory in Tubingen. For the simple Quick test the patients received, intravenously, 1·77 gm. of sodium benzoate in 20 ml. liquid (sterile ampoules having been produced by the firm of May & Baker). For the modified Quick test the patient was given 3 gm. glycine as well, half an hour before the sodium benzoate. Punctually one hour after the injection the patient emptied his bladder completely.

When the action of ACTH on the hippuric acid excretion rate was investigated, 25 mg. ACTH (25 int. units) were injected intramuscularly one hour before the intravenous injection of sodium benzoate. The ACTH was prepared in this laboratory according to Reiss and Halkerston (1950).

RESULTS.

Investigation results, after carrying out simple and modified Quick tests on the acute and chronic schizophrenics of our series, are recorded in Table I.

TABLE I.—*Correlation of Quick Test Results according to Duration of the Schizophrenic Disease.*

		No. of patients.	% excretion ± S.D.	" *t*."	Value for " *t* " for significance at *P* = 0·001.
Simple Quick test	Acute schizophrenia	11	57·9±6·3	10·3	3·65
	Chronic schizophrenia	54	34·3±9·9		
Modified Quick test	Acute schizophrenia	11	71·7±7·5	3·47	3·65 (2·85 at *p* = 0·01)
	Chronic schizophrenia	46	62·0±11·4		

The mean excretion rate of the acute schizophrenic patient was found to be 57·9 per cent. ± 6·3. This is in the same range as generally found on normal control persons (Quick, 1938; Neuweiler, 1939; Sherlock, 1946; Mall and Jünemann, 1952) and as also found during this investigation on normal control persons.

In all chronic schizophrenics however, the excretion rate is significantly decreased (34·3 per cent. ± 9·9) as compared with the acute schizophrenics.

Both groups of patients show considerable increases in the hippuric acid excretion rate (modified Quick test) after feeding with glycine (Table I). In all groups of schizophrenics the hippuric acid excretion rate rises to values which are in the normal range after feeding with glycine. There is hardly any significant difference between acute and chronic schizophrenics in the results of the modified Quick test.

While carrying out the investigations of hippuric acid excretion on this group of chronic schizophrenics we recalled that the same group had shown disturbances when tested for adrenal cortex responsivity, and was, in particular unable to mobilize ACTH endogenously in the glucose tolerance test, the reactivity of the adrenal cortex to injected ACTH being comparatively better preserved. Repetition of this test showed similar results, as already published by Reiss, Hemphill, Early, Maggs, Cook and Pelly (1951). A new investigation series was, therefore, started where 25 mgm. ACTH were injected before the intravenous benzoic acid injection. The results are compiled in Table II. It can be seen that treatment with this comparatively small ACTH dose, and in as short a time interval as one hour, was sufficient to raise the hippuric acid excretion rate by about 30 per cent. This increase is statistically significant.

TABLE II.—*Influence of 25 mgm. ACTH Injected One Hour before the Benzoic Acid on the Hippuric Acid Excretion Rate (simple Quick Test) of Chronic Schizophrenics.*

Pretreatment.	No. of patients.	% excretion ± S.D.	"*t*."	Value for "*t*" for significance at $p = 0·001$.
None	54	34·3±9·9	4·31	3·65
25 mgm. ACTH before benzoic acid	47	43·3±10·9		

DISCUSSION.

The results found in this investigation on acute schizophrenic patients appear to be at variance with claims made by Georgi and co-workers, and Mall and Jünemann. These authors however, did not differentiate in their statistics between acute and chronic cases, and it remains to be seen whether the acute cases investigated by these authors are not also on a place in the distribution diagram which overlaps considerably the normal range.

The difference in the detoxication ability in the acute and chronic patients appears of some importance towards the patho-physiologic explanation of the whole group of phenomena. One is reminded of the work of Golla (1929) who was able to show a general slowing down of many forms of activity in schizophrenic patients. Gastric secretion, specific dynamic responses to food digestion, respiratory response to CO_2; all these responses eventually occurred, but were very much delayed. Detoxication of benzoic acid and deterioration in detoxication ability in general, might be co-ordinated with the general slowing down of the metabolism as described in the work of Golla. It could be debated whether the development of an inability of the organism to mobilize efficiently ACTH endogenously in chronic schizophrenia does not play a primary rôle in these events.

Animal experiments carried out by Reiss and Gothe (1937) have shown that intramuscular injection of ACTH into rats considerably stimulates the activity of the reticulo-endothelial system and its ability to take up lithocarmin. It seems to the authors that the benzoic acid detoxication test is not so much a test for liver function as for the function of the reticulo-endothelium. This is well in agreement with the investigation results of Smith and Cousins (1953) carried out in this hospital, who have been unable to note any hepatic dysfunction in a study of 58 cases of various types of schizophrenia, and serial investigations in five cases of periodic catatonia. They used a combined clinical and biochemical assessment, the latter based on a battery of five tests—urinary urobilinogen, differential serum proteins, alkaline phosphatase, quantitative bilirubin estimation and thymol turbidity.

Summary.

Benzoic acid excretion tests were carried out on 11 acute and 54 chronic schizophrenic patients.

The hippuric acid excretion rate was found to be disturbed in the chronic schizophrenics but not in the acute schizophrenic patients.

Treatment with ACTH one hour before the injection of benzoic acid, increased the hippuric acid excretion rate significantly in chronic patients.

Some conclusions regarding the relationship of the benzoic acid detoxication test to liver function and adrenal cortex function in chronic schizophrenia are discussed.

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THE SIGNIFICANCE OF AMINO-ACIDS IN NEURO-PSYCHIATRIC DISEASES.

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The relationship of neuro-psychiatric disorders to electro-physiology and biochemistry has a vast literature, review of which is not within the scope of this preliminary report. The report itself concerns a study of an aspect of this relationship based on 30 unselected neuro-psychiatric cases. Each case had an electroencephalographic (E.E.G.) and a cerebrospinal fluid (C.S.F.) investigation, the latter with reference to the presence of amino-acids.

Before details of the investigations are given, the techniques and criteria of evaluation should be outlined. The majority of the E.E.G. records were taken with a 6-channel Ediswan machine, using eight varieties of montages (21 cases). Overventilation was carried out in all and photic stimulation in nine cases; nine of the records were obtained with the 4-channel Ediswan "portable" at Redhill County Hospital, Surrey. As to the evaluation of the records, a three-point scale of Normal, Abnormal and Severely Abnormal has been adopted, but it must be borne in mind that any differentiation between normal and abnormal records is arbitrary, and is based on obtained correspondences without a known theoretical basis. The records in this study have been evaluated as abnormal when there was a relative excess of medium to high amplitude theta, a marked fast activity and/or sharp waves; severely abnormal records denote in this evaluation those showing delta focus and severely disorganized or paroxysmal activities.

The assessment of amino-acids from the C.S.F. demands a more detailed description, since the method used might be subject to criticism. The paper chromatography method was employed, and the technique followed was that recommended by C. E. Dent (1951). Three ml. of C.S.F. was deproteinized by precipitating the proteins with ethanol; the centrifuged fluid was treated with three times its volume of chloroform and the deproteinized fluid separated. The fluid then was desalted, in the Shandon electrolytic apparatus, then passed through a No. 4 sintered glass filter to remove insoluble matter formed during desalting. One ml. of the fluid was evaporated and the amino-acids were extracted using three separate 0·1 ml. volumes of distilled water. This was then applied in 0·02 ml. amounts to the Whatman No. 3 mm. filter paper, for 2-dimensional chromatography. The amino-acids on the paper were treated in one direction with a saturated solution of water in phenol, dried and then treated in the other direction with n-butyl-alcohol with acetic acid and water. The dried paper was sprayed with ninhydrin to develop the separated amino-acids. The developed amino-acids were identified by their relative position, by their colour, and by calculating the R_F (ratio factor). In comparison with the control chromatograms the R_F, however, whilst reliable within one chromatogram, showed a considerable range within the whole group of chromatograms. The same fact was also observed by R. H. Horrocks and G. B. Manning (1949) when studying sugar chromatograms. They demonstrated that the differences were due to changes in temperature. The R_F, however, is only one means of identification, and identification within one chromatogram remains unaffected.

Subjects and Results.

The material consisted of 20 male and 10 female patients, all adults. Their average age was 51·2 (range 20–78). For the purpose of this preliminary investigation their diagnostic distribution has been grouped as follows :

Group A : Neuro-psychiatric conditions having a well-defined pathology and showing both psychiatric and neurological symptoms ; such were cerebral tumours, general paralysis of the insane, disseminated sclerosis with psychosis, etc., 9 cases.

Group B : Neuro-psychiatric conditions having a well-defined pathology and showing predominantly psychiatric symptoms. Such were senile dementias, including arteriosclerotic dementias, with no previous history of mental breakdown, 8 cases.

Group C : Neuro-psychiatric conditions, showing psychiatric symptoms only, and having no defined pathology. Such were chronic and sub-acute schizophrenics, neuroses, etc., 13 cases.

To begin with, the E.E.G. records were taken and evaluated. Then the C.S.F.'s were obtained and the presence of amino-acids ascertained. The latter investigation showed that various amino-acids were present, and that the variety of acids increased in number in certain cases. Four acids were identified in all cases : glutamine, glutamic acid, alanine and glycine. Tryptophane and valine were identified in the majority of cases. The remainder of the cases showed seven or more amino-acids present, some of which we were unable to identify. Thus inspection of the tables suggested that on the basis of the number of amino-acids present the patients should be divided into two groups, one group having various acids up to and including six in number and the other showing the presence of acids over that number.

The relationship between number of amino-acids present and abnormality of E.E.G. is set out in Table I. This shows that there is a definite correspondence between the occurrence of amino-acids in excess of six, and abnormal E.E.G. findings. The correspondence between severely abnormal E.E.G. findings and the presence of more than six amino-acids is even more definitely marked (see Table II), than when the E.E.G. findings are merely divided into normal and abnormal records.

The relationship of diagnostic status to the physiological findings is displayed in Table III. This demonstrates that Group A is characterized by the excess number of amino-acids and Group C by the lesser number, to a statistically significant extent. On the other hand, there is no statistically significant difference between Groups A and B and Groups B and C, in respect of the number of amino-acids present.

Finally Table IV demonstrates the correlations between the diagnosis and the severely abnormal E.E.G. findings. It shows that in this respect each group differs from the other to a statistically significant degree.

TABLE I.

Amino-acids.	E.E.G.		Totals.
	Normal.	Abnormal.	
Less than 7	11	6	17
Seven and more	3	10	13
Totals	14	16	30

$p = \cdot 03$.

p denotes the probability of getting by pure chance the obtained frequencies or frequencies showing a more extreme contrast. (Fisher, R. A., 1950.)

TABLE II.

Amino-acids.	E.E.G.		Totals.
	Normal.	Severely abnormal.	
Less than 7	11	1	12
Seven and more	3	6	9
Totals	14	7	21

$p = \cdot 01$.

TABLE III.

Amino-acids.	Diagnosis.			Totals.
	A.	B.	C.	
Less than 7	2	5	10	17
Seven and more	7	3	3	13
Totals	9	8	13	30

A *vs.* B $p = \cdot 12$.
A *vs.* C $p = \cdot 02$.
B *vs.* C $p = \cdot 89$.

TABLE IV.

E.E.G.	Diagnosis.			Totals.
	A.	B.	C.	
Normal	0	3	11	14
Severely abnormal	6	1	0	7
Totals	6	4	11	21

A *vs.* B $p = \cdot 03$.
A *vs.* C $p = < \cdot 001$.
B *vs.* C $p = \cdot 03$.

COMMENT.

The investigations show that the number of amino-acids in the C.S.F. averages five, all being quite distinctly recognizable and that this number increases in certain neuro-psychiatric illnesses. The establishment of any possible qualitative relationship between the various amino-acids and neuro-psychiatric symptomatology demands the investigation of large homogeneous groups of cases. The study also reveals a parallelism between an increased number of amino-acids and E.E.G. abnormalities. One is fully aware, that despite the use of the analyser, the evaluation of an E.E.G. record is to some degree subjective, and its validity would be strengthened if a similar evaluation were given by two or three independent interpreters. At least the subjective error here was constant; moreover, the category of severely abnormal E.E.G. is outside the margin of subjective judgment.

From the clinical point of view, of course, the relationship of the physiological findings to the diagnostic categories is of primary importance. One does not expect to find an answer to the problems presented by a single diagnostic category in a piloting experiment, based on 30 cases only. The shortcomings of the arbitrary diagnostic groups (A, B and C) are not only due to their relatively small numbers but, to some degree to their dyshomogeneous nature. In the eight cases of Group B, for instance (the senile group), five patients showed an abnormal E.E.G. and only one a severely abnormal E.E.G.; a comparatively high incidence of abnormal records. Group C, on the other hand, was a mixture of nine schizophrenias, three neuroses and one depression; they had two abnormal records, and no severely abnormal record at all, as Table IV shows. This is somewhat below the expected number of abnormal records within the schizophrenic group. Clearly it would be desirable to operate with carefully defined homogeneous groups in order to ascertain more accurate quantitative and qualitative interrelations between the physiological and clinical findings.

The question of homogeneous groups, however, raises the problem of psychiatric diagnosis, and the uncertainties, for example, of the various subclassifications of schizophrenia. On the other hand, in the present sample, the patients in Group A, all showed clinically a marked intellectual deterioration corresponding to the presence of excess acids and severely abnormal E.E.G.'s. Group B, from the point of view of intellectual deterioration occupied an intermediate position, but its position was less clear in regard to the number of amino-acids. These clinical and physiological findings suggest that investigations should be attempted that take as their correlative classification kinds and degrees of cognitive disturbance rather than the usual diagnostic entities. The present findings encourage us to undertake such investigations on a larger scale.

SUMMARY.

1. Various amino-acids were identified in the cerebrospinal fluid of 30 unselected neuro-psychiatric cases.

2. A statistically significant relationship was found between the presence of amino-acids in excess of six and the occurrence of an abnormal E.E.G.

3. The patients with an increased number of amino-acids in their C.S.F. and a severely abnormal E.E.G. showed clinically a marked intellectual disorganization.

We wish to thank Dr. J. P. S. Robertson for some help in statistical matters ; Mrs. B. Eisner for the E.E.G. recordings ; and the physicians at Redhill County Hospital whose patients are included among the cases reported upon.

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PERSONALITY STRUCTURE IN PSYCHOTICS BY FACTORIZATION OF OBJECTIVE CLINICAL TESTS.

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1. Aims: Personality Tests Designed from Structure.

To research workers in personality measurement the advance of routine testing procedures in clinical psychology has seemed peculiarly sluggish. Whereas solid theoretical foundations have been found for an account of the normal personality structure in factor analytic terms (5, 6, 7) and a rich variety of new tests has been created (8, 9, 14), the clinicians have confined themselves to one or two " gadget " tests, conceived with no more explicit relation to personality structure than a patent medicine has to modern physiological principles. The present research aims to bring factor structure measurement in a clinical population into relation with that found in normals and to provide a first, reproducible, test battery covering at least a dozen factors for use in clinics able to give sufficient time for valid and reliable measures of the primary personality dimensions.

No fine finish must be expected in either of these pioneer efforts. For in regard to the meaning of the factors, further work is required to relate the objective test patterns to rating and questionnaire syndromes, as well as to clinical diagnoses. By contrast, in the realm of normal personality, these relations already exist and we can indicate factor measurements corresponding to ego strength, schizothymia, super-ego strength, anxiety level, etc. (12, 14). However, a contemporary article (15), by relating the present factors more fully to those found in normal populations (and one other clinical population) integrates the present factors into that larger realm of meaning with some degree of certainty. As to the test battery itself, it is bound to be more cumbersome than the relatively brief and invalid gadgets now used in clinics, at least until some years of use have shown how to trim its more uncouth features without reducing the essential volume of information which it carries.

The aim of this research is thus a dual one: to determine factor structure in a clinical population by the same personality tests as have been used with normals, thus permitting comparisons; and to produce a test battery for the unitary dimensions found. Quite apart from the need to use a set of personality tests which can be expected to carry " factor markers" to key the present factors into those in a series of four other interrelated studies (8, 9, 14, 15), the choice of tests has to be dictated also by the compatible aim of representing the whole " personality sphere " (5).

Since the personality sphere rests logically upon a population of ratings (6), i.e., clinical-type observations, the objective tests have been created to test hypotheses about the nature of the functional unities found earlier in ratings (5, 6, 7). Indeed a history of study of the preliminary findings (6) in rating, questionnaire (12) and objective test (5) factors underlies the particular choices of tests and the kind of behaviour responses embodied in new tests. The requirements for the tests invented here are therefore that they shall show great catholicity, comprehensively representing most areas of behaviour and that they shall represent hypotheses about known factors. Only on such a basis can a factor analysis achieve the end of revealing personality structure, i.e., of showing the functionally independent behaviour patterns of greatest relevance in explaining general behaviour. Space precludes presenting here any further discussion of the test designs than can be given in Section 2, below; but it will be realized from inspection of the tests that the centre of effort in this research has been the creation of a range of new personality tests according to explicit psychological principles.

2. DESIGN AND LIST OF TESTS.

The research design consists in giving 102 distinct test measures, as listed below, to an assorted mental hospital population of 100 cases, mostly recorded as psychotics. The tests are then intercorrelated and the matrix is factor analysed. The factors thus found are "blindly" (i.e., without prejudice from earlier interpretations) rotated until a simple structure position is found. This is considered to offer the scientific as distinct from the merely mathematical explanation of the observed correlations. The factors in this unique solution position are then examined for meaning in the light of the pattern of variables which they most strongly load. These steps are now set out in detail.

Beginning with the list of variables used, we indicate them according to two index systems; on the extreme left the serial number in the present correlation matrix and, in the next column, the "Master Index Number," i.e., the number by which the test can be located in the whole group of researches as organized in this laboratory (8, 9, 14, 15) and by which the test will be referred to in future fuller discussion. Immediately after the title of the test is given the consistency coefficient (split-half reliability) where the test permits it to be calculated.

Brief Description of Tests.

Matrix Number.	Master Index Number.	Test Descriptions.
1 .	157 .	*Number of Jokes Overtly Reacted to as Funny.* The sum of rating points for S—'s laughter reaction to jokes told on a phonograph record: 1 point for negative reaction, 2 points for no response or neutral, 3 points for smile, 4 points for great laughter. Score is total of points. This score in non-psychotic populations was slightly different: subjects' ratings. Hypothesized Factor A (6).
2 .	2c (171) .	*Hidden Pictures: Lack of Rigidity.* S— instructed to look for "hidden pictures" in standard multiple perception tests (2) of 5 pictures. Any alleged picture accepted ("flexible key").

Matrix Number.	Master Index Number.	Test Descriptions.
3	158	*Increase of Tempo Under Threat.*—In myokinesis (drawing 1 inch lines blindfold) time was taken for S— to draw 20 lines (*a*) normally, (*b*) under shock if badly estimate. (No. 66 below.) Score is increased speed under shock.
4	153	*Cursive Miniature Situation Test:* (4) *Speed of Decision Group form of test.* $R = 0{\cdot}69$. Total number of decisions made, i.e., right and wrong decisions in 4 minutes.
5	15	*Cursive Miniature Situation Test: Excessive Use of Circles.* $R = 0{\cdot}82$. Group form of test: Number of circles used in emergencies beyond prescribed six (4). Hypothesized Factor I.
6	154	*Cursive Miniature Situation: Slanting Lines.* This is a simple count of slanting lines crossed and is a measure of failure to follow instructions. Found previously to be significantly higher in delinquents (4). Hypothesized factors C— and G—.
7	43 (i) (305)	*Ratio of Reaction on Mental to Physical Stimuli on P.G.R.* $R = 0{\cdot}72$. Ratio of mean conductance change for 7 disturbing mental (words, pictures) and 5 disturbing physical stimuli.
8	145	*Adaptability of Aspiration Level (in Coding).* Eight repeated code substitution tests in which response of A.L. between n^{th} and $(n+1)^{\text{th}}$ is related to degree of success in n^{th}. Formula: $\frac{\Sigma(c-a)}{\Sigma(b-a)}$ where a = initial estimate, b = us. completed after estimate a. c = estimate for second trial after doing b. Factor C.
9	100	*Optimism Over Doing Good.* Presented as test "Judgment of Human Nature" in which S— rates "workableness" of 30 "reforms." Hypothesis that genial optimism on human nature is measured of Factor A+.
10	25	*Ratio of Emotional to Non-Emotional Recall.* $R = 0{\cdot}41$. Immediate memory for sets of phrases, some emotional, some dry. (Modified from words in (9).) S— forewarned. Hypothesized as index of ego strength Factor C.
11	115 (i) (193)	*Ego Weakness 1:* $R = 0{\cdot}68$. *Suggestibility Shift from Unsuccessfuls.* As Test 14 in intention and Test 12 in content. S—'s attitudes are measured on a wide array of topics. Later they are re-presented with indications of what "unsuccessful people" choose. Shifts away are measured, i.e., tendency for subjects to lose independence and imitate "successfuls" on retesting. Factors C and G.
12	31 (iv) (184)	*Fluctuation of Attitudes: Material* 1. This measures a spontaneous, unstable shift of attitude when re-presented after one day. Scored on material of Test 11, by simple, non-algebraic, i.e., directionless addition of shifts. Tests 14, 16 and 18 are similar. Factors A and C— (3).
13	115 (ii) (194)	*Ego Weakness 2: Avoidance of Designated "Neurotics" Responses.* $R = 0{\cdot}69$. As Test 11 measure on lack of ego strength and independence as shown by number of shifts, on retest, away from responses designated as those of neurotics. (But not actually so.) Factors C and G.

Matrix Number.	Master Index Number.	Test Descriptions.
14	31 (iii) (183)	*Fluctuation of Attitudes. Material* 2. A similar measure to Tests 12, 16 and 18, but on material of Test 13.
15	34	*Immaturity of Opinion.* $R = 0\cdot77$. Change of opinion on re-presentation of same attitude test with new facts. Scored in direction indicated by presented facts, which should have been thought of earlier by a mature person. (As in (9) and (14).)
16	31 (ii) (182)	*Fluctuation of Attitudes. Material* 3. Similar to Tests 12, 14 and 18, but on Test 15 material.
17	35	*Suggestibility to Authority.* $R = 0\cdot75$. As in (9) and (14) (Sl. mod.) change of opinion (sum of shifts on 5 point scale) on re-presentation in direction of intervening "authority opinions." Material was first presented as bare statements and on second day as actual quotations from authorities. Factor E.
18	31 (i) (181)	*Fluctuation of Attitudes. Material* 4. As Tests 12, 14 and 16, but on Test 17 material.
19	96*a* (188)	*Little Effect of Frustrated Preference on Computing Speed.* Subject starts two calculations (one addition, one subtraction) and indicates his preference for continuing one of them. Despite wishes he is given the other. Ratio of computing speed after frustration to previous speed is measured. Intended for frustration tolerance measure. C factor.
20	96*a* (187)	*Effect of Frustrated Preference on Reading Speed.* Situation repeated as in previous Test 19 but measured alternatively by two stories and ratio of pre- to post-frustration reading speed.
21	155	*Range of Flicker Fusion.*—Standard flicker fusion apparatus (strobotac, with opal screen) in darkened room. Difference between highest number at which fusion reported and the lowest, i.e., a range of uncertainty score.
22	5	*Ratio of Regularly Warned to Irregularly Warned Reaction Time.* $R = 0\cdot70$. Six runs of 10 reactions each, even runs having a regular two-second warning, odd runs irregular warning interval. In (8) Derivation of Tests 23 and 24 here.
23	4 (175)	*Mean Reaction Time with Regular Signal.* $R = 0\cdot90$. In (8) Thurstone's perceptual factor (21). See Test 22.
24	4 (176)	*Mean Reaction Time with Irregular Signal.* $R = 0\cdot90$. In (8) Thurstone's perceptual factor (21). See Test 22.
25	30 (134)	*Ratio of Criticism of Self to Criticism of Other.* As in (9) S— gave "approvals" and "criticisms" (inventive, not selective) of self, home town, art, etc. Approvals neglected ; ratio of criticism of self to things not in-self sentiment.
26	156	*Lag of Flicker Fusion.*—Fusion point was picked up on four downward and four upward runs. This is differences of former and latter—a measure of "lag" in decision.
27	28	*Dynamic Momentum.*—As in (9) S— works as long as he wishes on anagrams, on increasingly difficult reading, as drawing a house. Time spent on each (instead of switching to new before exhausting old). Factor G hypothesized.

Matrix Number.	Master Index Number.	Test Descriptions.
28	148	*Aspiration for Improvement.* $R = 0\cdot91$. Score is number of coding tasks completed on a page taken from *subsequent* estimate of his performance for next time. Eight times.
29	147	*Estimated Breadth of Experience and Accomplishments.* On 30 questions covering wide range of experiences, hobbies, skills, subject indicates his degree of familiarity and skill. Factor K.
30	26	*Ability to Handle Surprises, Riddles.* $R = 0\cdot89$. As in (8) and (14) score on solving 30 riddles in 5 minutes, as index (negative) of "ideational rigidity" factor (11) and general intelligence (3). Factor B.
31	106	*Unreflective Acceptance of Unqualified Statements.* Subject checks out of 39 statements (most somewhat ambiguous or really needing qualification) those he will endorse as "*absolutely certain.*" Presumed Factors F, G−, and K−.
32	7	*Speed of Perceptual Closure.* $R = 0\cdot82$. Twelve uncompleted (Gestalt) pictures and 12 uncompleted words. (Score : number *completed* in 70 sec.) (cf. Test 33). In (14). Used to represent Thurstone's perceptual factor (21).
33	146	*Accuracy in Perceptual Closure.* Same data as Test 32. Number correct divided by number completed. Possibly Factor F.
34	396 (136)	*Ratio of Color to Form in Sorting.* $R = 0\cdot45$. As in (8) and (14) but presented to group by slides (colours consequently not exactly reproduced). Essentially a sorting in which neither colour nor form is an entirely adequate guide.
35	151	*Longer Time for Decisions on Principles than on Particulars.* Items in which decision is between generalizations are compared with those of a factual and particular nature. Hypothesis that K+ will do better at former and possible C+.
36	24*a* (180)	*Ratio of Initial to Later Performance : Reading Backwards.* $R = 0\cdot68$. Scored on 1st to 3rd minute's performance on task of reading sentences printed backwards. Factor G.
37	125	*Ratio of Personal to Institutional Values.* Items devised to distinguish adherance to internal conscience values rather than conventions and habits of social group. Factors I and K.
38	152	*Tendency to Agree* 1. (*Difference Score*). $R = 0\cdot80$. Tendency to *agree* to propositions regardless of subject matter. (Mainly on attitudes in optimism-pessimism test.) Scored as number of times S— said "agree" minus number of times S— said "disagree."
39	97	*Time Interval Perceived Longer During Ergographic Work.* $R = 0\cdot91$. S— estimate of time while pulling hard on ergograph to exhaustion was divided by the actual time.
40	656 (139)	*Logical Consistency of Attitudes.* Three parts of each of number of syllogisms scattered among attitude statements on controversial matters. Improved from (14) but still short of requirements of (1) incontestable logicality and (2) equal chance of scoring. Intended as measure of personality integration and Factor C−. Scored in direction of consistency. (One point for each set of 3 internally consistent.)

Matrix Number.	Master Index Number.	Test Descriptions.
41	—	*Random Variable.* A set of random numbers assigned to subjects, to test properties of the factorization, notably the standard error of a loading.
42	—	*Random Variable.* A second, independent set of random values.
43	103 (i) (191)	*Low Amount Considered Possible in Given Time for Others.* $R = 0.40$. Subject asked to estimate for people generally how much time required for completing 20 varied tasks (selective answers). Factor G− or F+.
44	13	*Oscillation.* $R = 0{\cdot}62$. Variation in successive 7 sec. periods of performance on cancellation, checking, etc. (In (8).)
45	103 (ii) 192	*Low Amount Considered Possible in Given Time for Self.* $R = 0{\cdot}42$. As Test 43, but estimate of time to do things oneself. Presumed Factor E+ and G+.
46	119	*Artistic Taste in Colour-Blending.* $R = 0{\cdot}29$. Number of right choices on 30 paired choices of good and bad colour combinations (as judged by artists) divided by number of choices made. Factor I and possibly K.
47	108	*Self-Confidence on Untried Performances.* $R = 0{\cdot}89$. Second part of Test 29 in which subject is asked how well (3 pt. scale), with practice or opportunity, he would *expect* to master each of a variety of accomplishments he states he has not tried. Factor E or O−.
48	114	*Underestimation Prospective Performance in Unexpectedly Difficult Material. (Judging lines and dots, answering intelligence and information questions.)* $R = 0{\cdot}86$. Number of problems done on a page of material minus the *prior* estimate of the subject as to how many he would do. Total score is sum of these differences. i.e., discrepancy between estimate and actual performance. Factor E.
49	105	*Tendency to Perceive Threatening Objects.* $R = 0{\cdot}86$. S— presented with 16 vaguely sketched collections of objects and asked to identify them. Scored on proportion of dangerous objects (weapons, storms, pitfalls, etc.) to benign objects seen.
50	112	*Ratio of Adverse to Favourable Self-Reference in Events.* $R = 0{\cdot}64$. In a list of world events S— is asked to say which may affect him personally and whether favorably or unfavorably. Ratio of u. to f. in latter. Factor L.
51	109	*Ratio of Pleasant to Unpleasant Associations.* Subject lists in four 2 min. periods (*a*) unpleasant past, (*b*) pleasant past, (*c*) unpleasant anticipations, (*d*) pleasant future anticipations. Score = $b/a + d/c$. Factor F.
52	110	*Anteversion-retroversion Ratio.* Re-arrangement of data for Test 51 as $c/a + d/b$. Factor F.
53	29 and 133	*Criticalness (Severity) of Judgments.* As in (8), judgments of various presented human performances, e.g., drawings that could be graded by S— with varying severity. Presumed part of severity or hostility from Factor A− or E (dominance).

Matrix Number.	Master Index Number.	Test Descriptions.
54	116	*Cynicism or Hard-headed Judgment.* $R = 0 \cdot 89$. Number of items checked on hard-headed versus sentimental social issues, e.g., such as realism about reformability of criminals, " copy book headings " versus " easy idealism." Variously evaluated as realism, cynicism, severity, by experimentors. Factor I.
55	117	*Fashionable Good Taste in Social Matters.* A test of information about upper class or " approved " furnishings, eating, reading, etc., tastes. Intended as measure of K+ factor.
56	118	*Sense of Poetic Aptness.* A test of ability to choose better completing lines for incomplete poetry (rare, but authentic examples, selective answers). Factors I and possibly K.
57	107	*Knowledge of Etiquette.* $R = 0 \cdot 84$.—Twenty-four multiple choice items on *savoir faire* on assumption this is K factor.
58	104	*High Estimation of Personal Worth.* Subject asked to check " self-inventory " containing mixed esteemed and disapproved traits. Scored on high percentage of " desirables " possessed.
59	2 (198)	*Lack of Perceptual Rigidity, Hidden Words.* In (11). Subject to find word hidden in random order of letters composing the word. Four one-minute series of 10 each.
60	99	*Ratio of Verbal to Numerical Ability.* $R = 0 \cdot 68$. Thurstone measures, summed in Test 61, treated as ratio here. Assumption verbal ability associated Factor N.
61	11*b* (130)	*Intelligence : Verbal and Numerical Ability.* On Primary Mental Abilities Test.—As a marker for intelligence factor (B+ in personality series).
62	101	*General Deficit of Aspiration Level Relative to Performance, in Coding.* Sum of differences between (*a*) number completed on each of 5 first pages and (*b*) aspired number for second pages. (*a–b*)'s added with respect to signs for all 5.
63	124*b* (195)	*Tendency to Agree 2. (Ratio : Optimistic Statement Material.)* (Ratio Score.) Same as 38, but scored as ratio instead of difference.
64	122	*Static Ataxia.* (S. Mod.) Measured by sway (differences of extremes in any direction) as in Test 73 but without suggestions. Factor C−.
65	98 and 143	*Cursive Miniature Situation Test : Absolute Number Correct Decisions.* As Test 78 but scored absolute number of decisions correct.
66	95	*Myokinetic Movement Decrease under Threat.* Repetition of Test 3, i.e., Myokinias when told there would be " punishment " for poor estimates by shocking (done anyway on two predetermined lines out of 10). Ratio of 20 normal to 20 threat lengths.
67	91	*Autistic Suspicion.* Subject under a sheet in room of spectators scored on frequency with which he stated people were pointing at him (being told they would point some of the time). Tried for paranoid Factor L.

Matrix Number.	Master Index Number.	Test Descriptions.
68	38*b* (135)	*Ratio of Consonant to Dissonant Opinions Recalled.* $R = 0{\cdot}60$. Ratio, among recalled attitude statements, of those agreed to those disagreed with. Marker for a factor of "rigidity-low energy," presumably H−, as in (8) and (14).
69	41	*Two Hand Co-ordination.* $R = 0{\cdot}91$. Exactly as in (8) and (9), to mark Thurstone's perceptual factor (21).
70	21	*Absence of Questionable Preferences.* $R = 0{\cdot}89$. Defined in (8) and slightly modified since by item analysis choice of decent versus trashy reading. Factor G+ or K+.
71	36	*Ability to State Logical Assumptions.* $R = 0{\cdot}40$. As in (8) and (14), from Watson-Gläser test (23). Factor I.
72	93	*Little Effect of Restraint on Performance.* Subject counted number of shapes in complex figures under (*a*) normal conditions, (*b*) when clamped in physical restraints. Hypothesis that performance of neurotics (C−) more affected by restraint.
73	42	*Body Sway Suggestibility.* As in (8) and (14) and Eysenck (17). Distance between extremities of sway. Marker for Factor C−, presumed general neuroticism (17).
74	94	*Mean Frequency of Flicker Fusion.* $R = 0{\cdot}93$. Mean of 10 up and down runs, with constant distance and illumination, on strobotac (see Test 21). As measure of rigidity Factor shown in (11).
75	8	*Rate of Alternating* (*Cube*) *Perspective.* $R = 0{\cdot}82$. In (8). Usual design. Not forcing but allowing fluctuation.
76	22 and 131	*Ratio of Chance to Purposeful Observation and Memory.* Defined in (9), but slightly modified and scored here in the opposite direction. S— performs task and recalls according to instruction, but is also test on recall of "irrelevant" matters. Factor H+.
77	46 and 137	*Impairment of Unseen Maze Performance by Discomfort and Threat.* $R = 0{\cdot}79$. Subject had four runs on unseen pencil maze, instructed to get as far as possible in given direction. In the two middle runs he was given electric shock (but not told that the forthcoming shock would be a punishment for poor performance). Score is ratio of distance covered in runs 1 and 4 to runs 2 and 3. Presumed F− and H− factors.
78	98	*Cursive Miniature Situation Test: Correctness of Decision.* ($R-W$.) $R = 0{\cdot}69$. As in Test 65 but scored on decisions per minute, right minus wrong.
79	92	*Low Readiness to "Initiate Animal Sounds."* Subject instructed in individual test to "make a noise like a cat" and so on. Mean time to respond to instruction, as measure of embarrassment. Factor H.
80	43	*Magnitude of Mean P.G.R. Deflection.* $R = 0{\cdot}74$. As in (9) and (14), mean percentage conductance to 12 physical and mental stimuli. For Factor H.
81	113	*Little Breakdown of Reality Principle.* $R = 0{\cdot}56$. Subject checks "time" items in wide range of beliefs scaled to be expressive either of reality function or of artistic thinking (pleasure principle, wishful thinking, irrational fears, ego defence distortions). Factor C−.

Matrix Number.	Master Index Number.	Test Descriptions.
82	83	*Fidgetometer Frequency.* $R = 0{\cdot}88$. As in (9), best with record of body as well as foot movements. Number per minute during middle (Myakinesis and Distraction) part of individual test session.
83	161	*Ratio of Performance (Cancellation) under Approval to Disapproval.* Comparison of speed and accuracy in one period when examiner said "Good, good" with one period when he said "You are doing poorly." Factor E.
84	162	*Ratio of Performance (Cancellation) Normal to Shock.* In one period of 30 sec. S— performed at normal top speed and in one other sandwiched between, with shock administered regardless of performance. Factor I.
85	163	*Ratio of Performance (Perceptual Closure) Under Approval to Disapproval.* As Test 83 but Test 32 material used. Factor E.
86	164	*Ratio of Performance (Perceptual Closure) Normal to Shock.* As Test 84 but with Test 85 type of material. Factor I.
87	165	*Ratio of Performance (Classification) Under Approval to Disapproval.* As 83, 85, but on performances picking one work from a group of 5 which does not belong with the general concept in the remaining 4. Factor E.
88	166	*Ratio of Performance (Classification) Normal to Shock.* As 84, 86 but on classification. Factor I.
89	150	*Extremity of Viewpoint. Material* 2. As in (14). Identical with 98 except for different material (that of Test 90). Ratio of responses "absolutely" agree and "completely" disagree to "partly" agree or disagree. Factor C.
90	150*b* (196)	*Agreement with Platitudes.* $R = 0{\cdot}91$. After checking on a set of platitudes (not labelled as such) which remarks seemed so obvious as not to be worth saying, S— was asked how much he agreed with each remark. Score is number of items agreed with or partially agreed with divided by number of items disagreed or partially disagreed with.
91	2 (i) (172)	*Motor Rigidity. (Perseveration).* $R = 0{\cdot}30$. Test 1, page 234 in (2) Factor C—. (5.) Letters written with backward movement.
92	2 (iv)	*Motor Rigidity. (Perseveration.)* $R = 0{\cdot}24$. Test 2, page 235 in (2). Factor C— (5.) Words rewritten doubling letters.
93	2 (ii) (173)	*Motor Rigidity. (Perseveration.)* $R = 0{\cdot}33$. Test 5, page 239 in (2). Factor C—. (5.) Personal name written backwards.
94	2 (iii) (174)	*Motor Rigidity. (Perseveration.)* $R = 0{\cdot}21$. Test 6, page 242 in (2). Factor C—. (5.) Numbers written backwards.
95	6 and 177	*Ideo-Motor Speed.* Sum of speed scores on parts of 2-hand co-ordination test (with 2-hand co-ordination partialled out) plus sum of five writing speed scores rigidity test (with rigidity ratio eliminated).

Matrix Number.	Master Index Number.	Test Descriptions.
96	120	*Ratio Inaccuracy to Speed.* Sum of errors-over-number-done fractions for oscillation (Test 44), mazes (Test 77), closure (Test 32), cancellation (Test 83) and classification (Test 88), and two-hand co-ordination (Test 69).
97	167	*Immediate Memory Efficiency.* S—'s recall on a variety of intellectual material was scored by pooling total amount recalled, in immediate reproduction or recognition on subtests, covering attitude statements. Factors J− and perhaps H+.
98	67*b* (141)	*Extremity of Viewpoint. Material* 1. As in (14), ratio of "absolutely true" and "absurd" checks to more moderate alternatives on 100 attitude statements used elsewhere. (Cf. Test 89.)
99	326	*Ratio of Errors to Attempts.* In memory test the numbers of items erroneously recalled, divided by the total number of attempted recollections.
100	111 (i)	*Amount of Self-Reference in General Events.* Score = affect favourably plus affect unfavourably divided by total number of items, in Test 50. Factors E and L hypothesized.
101	126	*Ratio Male to Female Person Choices.* $R = 0{\cdot}55$. Presented as (*a*) "artistic" preferences in presented male and female sculptures and (*b*) "conversation" preferences in male and female portrait comparisons. Scored: Men in (*a*) and (*b*). Women in (*a*) and (*b*) Masculinity factor (5).
102	62 (138)	*Ratio Emotionally-Interesting to Emotionally-Dry Reading Speed.* Ratio of normal reading speed on four passages; two gripping, two dull, when instructed to read quickly. For Factor G−.
103	25*c* and 132	*Ratio of Emotionally-Interesting to Emotionally-Dry Recall.* $R = 0{\cdot}23$. Differs from 10 (and has lower reliability) in that four actual stories rather than a word list. Recognition scores for ideas in strongly emotional stories divided by words recognized after emotionally-dry, intellectual, lecture material. Presumed test of Factor G−.
104	3*b* (127)	*Speed of General Judgment.* $R = 0{\cdot}73$. Not on intelligence-demanding items but on a *variety* of opinion statements. Instructed to work quickly. Factor F.

It should be noted that the above 104 variables are actually derived from 76 tests, and that usually when two or three variables derive from one test they do so in a manner which minimizes common error variance (no "apparatus" or "common error" factors are found in the following factorization). *More* than 76 tests were originally given, but except for variables 103, 109 and the rigidity measures, which claim special psychological interest, tests were dropped which had consistencies below 0·4 or which proved in experiment to be unsatisfactory for any other reason. These included a test of Effect of Fatigue in Increasing Weight Estimate; Motor Speed; Tempo; Willingness to Fight

TABLE I.—*Rotated Factor Matrix.*

Variables.		Factors.																		
Present Matrix Number of Variable.	Master Index Number.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	*h*².
1	157	28	−11	17	−13	−00	11	−00	−05	−00	21	00	−10	55	04	−08	−07	−01	−29	64
2	2*c* (171)	−01	29	09	03	−09	−19	−04	−08	01	−15	−07	−10	02	−24	−04	−01	22	00	33
3	158	−07	−12	−10	−08	08	11	−06	26	20	14	−03	06	−05	−00	24	−25	−09	−03	36
4	153	53	41	−20	13	01	14	−18	01	21	−01	−06	19	04	−10	−01	−05	07	15	56
5	15	25	77	−07	10	01	18	00	10	−10	−13	04	−09	−16	−03	−04	−18	11	02	98
6	154	10	01	−02	13	−05	−02	−16	−16	−15	01	−02	04	−16	01	12	−14	−05	−05	18
7	43 (i)	−02	06	−31	−15	01	21	−09	−06	−13	−07	01	−07	−11	−04	−01	−07	−01	−39	35
8	145	20	−00	13	−21	−03	01	20	−10	−07	−11	18	−09	19	−01	01	−06	09	14	31
9	100	−04	−21	−25	−13	−09	−11	−12	−05	−21	03	03	−27	−01	−03	12	−03	05	−13	43
10	25	04	−20	−23	40	−03	14	−12	−07	−11	10	09	−10	09	−02	−00	−26	−01	01	43
11	115 (i) (193)	−34	15	−09	−39	09	05	32	04	07	18	−10	−04	14	−11	14	−06	−05	−20	52
12	31 (iv)	01	−06	22	22	−12	−58	−15	−08	−06	−08	04	17	−11	−16	−11	−00	05	−01	76
13	115 (i) (194)	−10	04	−04	07	19	00	32	−07	14	04	04	06	−10	−07	01	−17	03	12	31
14	31 (iii)	−07	07	27	−02	03	−62	−04	03	−02	15	−14	34	03	00	03	10	05	01	77
15	34	−06	07	03	10	21	−13	08	−03	02	−04	26	−18	−04	−15	−66	−14	−04	−09	64
16	31 (iii)	20	−06	01	22	11	−57	−09	−12	11	−13	−03	49	01	09	12	−04	−08	17	85
17	35	−01	−01	−11	−26	−22	17	−04	05	02	12	−34	32	12	−04	−28	04	04	−06	49
18	31 (i)	−02	−03	05	−04	−34	−11	−26	03	07	03	−06	46	−07	−06	−12	07	04	13	53
19	96*a* (188)	−04	32	05	−71	15	02	−15	08	−07	15	−07	−16	08	−02	−10	16	−08	−03	68
20	96*a* (187)	−25	−24	12	−24	−13	−15	20	13	05	01	17	−09	03	11	−06	−05	−09	−03	39
21	155	−26	−09	00	−11	04	−02	−07	05	−11	24	−38	32	−33	48	12	−07	39	00	90
22	5	−02	07	00	−00	12	−04	−08	10	25	09	00	−08	−00	−03	−00	05	38	02	26
23	4 (175)	−47	01	12	−00	−28	10	10	−01	08	05	01	49	−10	−04	06	−22	01	04	76
24	4 (176)	−46	−01	08	−07	−27	11	10	−04	01	00	00	52	−05	−02	07	−22	−19	03	79
25	30 (134)	−11	−04	−01	02	−04	−14	−18	−13	−35	−12	−22	−18	26	−07	01	−23	03	12	53
26	156	−12	−06	−00	24	11	07	−14	−12	−08	−03	−25	30	−36	16	12	−12	14	−02	48
27	28	−27	00	−04	−04	04	02	36	−10	01	39	07	−13	−06	36	−15	05	−24	−05	60
28	148	−54	−17	03	03	−09	−06	−01	−05	−03	34	−03	13	05	−11	−03	−19	02	−12	49
29	147	06	18	04	02	−20	−16	−21	−03	06	04	−07	−22	09	−11	−26	−05	−09	22	41
30	26	50	05	18	03	21	−18	09	06	−17	−02	09	−50	00	−02	−01	−03	−02	12	73
31	106	−03	17	−13	−19	−61	−10	−10	25	−06	03	−02	−17	−04	12	04	−09	−05	−21	86
32	7	21	17	21	14	01	−21	38	−19	05	01	−19	−25	01	−07	−21	08	−10	03	55
33	146	−01	−27	07	15	28	−19	14	13	−00	−08	12	−21	−15	18	−09	20	−14	−08	37
34	396 (136)	−39	−30	−09	−23	08	22	−17	21	−11	09	−12	16	−01	−19	17	−16	00	−13	54
35	151	04	01	−11	−09	−01	15	27	09	−04	−10	−26	08	−12	−07	13	05	−30	−04	38
36	24*a*	−10	00	−27	−24	−01	−13	05	−02	06	21	−12	19	10	16	17	10	−21	14	43
37	125	23	−15	19	−02	17	−13	05	−02	02	08	−18	16	−05	−14	−13	11	12	25	48
38	152	−04	−33	15	24	−39	−08	00	06	−06	04	35	−04	04	−03	06	03	−03	18	57
39	97	−00	−06	−07	16	−09	−09	05	05	30	−06	−51	40	−02	02	09	11	07	−20	51
40	656	−02	−14	15	04	−33	−25	−05	22	07	07	07	−23	−23	11	−01	19	−10	−11	48
41		−08	−00	07	09	10	05	16	32	−29	06	08	08	−07	−09	−03	−04	01	−06	37
42		−08	−03	29	09	−07	12	−03	06	−30	21	19	−05	−02	08	−08	46	−10	11	60
43	103 (i) (191)	47	15	−16	11	05	−11	03	−00	19	−10	−17	−04	−04	14	−06	−04	14	−22	52
44	13	21	23	−04	−27	01	08	−07	07	−10	−22	−07	02	38	04	41	02	10	01	60
45	103 (ii) 192	21	10	44	27	15	−40	19	−07	00	−45	27	−57	−06	−09	04	08	−04	−08	96
46	119	−00	01	16	17	−06	−05	02	03	10	−14	−07	−21	21	01	−03	−14	19	−22	23
47	108	03	45	−01	−18	−13	15	11	−12	09	25	09	−02	02	−07	01	−16	−19	−15	48
48	114	15	18	23	09	−01	−13	−42	21	−22	11	10	−08	−09	18	−14	−02	−04	07	51
49	105	22	−03	−03	−14	09	−05	−03	40	07	−04	−10	−14	−15	−07	07	02	−01	−25	41

50	112	06	−02	38	03	06	10	−35	34	−35	28	−04	−18	−19	−30	−00	00	11	[illegible]	[illegible]
51	109	22	−05	−03	−06	−04	−09	−15	14	−38	08	−06	−16	−01	−45	−04	00	05	08	65
52	110	33	14	08	18	−07	07	−16	−16	−27	15	01	−05	06	−33	−07	−05	05	07	46
53	29 and 133	44	15	−1	04	−04	15	−16	01	18	−09	−06	07	−25	−13	−14	−09	04	−04	44
54	116	−11	33	−01	−10	−11	−06	00	07	33	10	−46	34	03	13	04	10	11	−22	51
55	117	30	06	05	00	30	−02	16	−11	−01	11	−14	−17	04	20	01	−48	−21	−03	81
56	118	31	−10	23	19	−06	05	01	−17	−00	27	−11	11	−12	−04	03	−21	−04	18	48
57	107	34	−01	−02	−06	07	06	11	24	−05	−13	27	−57	−14	−12	−15	−13	13	−09	62
58	104	12	29	−19	−16	−19	03	−17	01	17	01	09	−11	06	−15	−08	−11	02	06	32
59	2	44	24	06	−04	01	−02	−07	30	−06	−13	−02	−49	00	09	06	15	02	04	77
60	99	09	03	31	09	−08	−06	03	09	−27	22	03	−28	00	−04	−13	−35	−02	09	43
61	116 (130)	57	25	03	−10	04	17	17	03	−05	110	01	01	03	04	10	−02	−05	17	57
62	101	−14	07	−06	10	00	−16	−02	11	−12	−01	25	−18	10	−22	15	−01	03	−29	45
63	124*b* (195)	−01	−40	−04	10	−68	02	05	−39	10	21	02	04	−01	12	10	03	−04	−05	91
64	122	−09	02	−01	21	−27	−03	01	07	01	01	12	04	21	−08	−09	−14	−05	35	42
65	98 and 143	53	19	−30	16	09	12	−08	01	45	−08	19	−10	−09	−38	−01	−03	14	05	88
66	95	07	−23	−16	09	01	01	−09	18	17	−03	−08	00	−05	29	20	07	38	01	38
67	91	−03	03	−06	17	−12	−05	08	−53	−07	−09	21	−21	−04	−04	−01	−05	12	−12	47
68	38*b* (135)	−01	05	04	16	−39	−10	−04	21	−13	15	02	−08	03	−01	13	−24	16	−01	49
69	41	−18	−09	05	−10	−06	−24	37	12	16	01	11	−10	01	−01	02	14	−05	09	32
70	21	−05	−08	−15	−01	−11	−21	−05	−10	24	05	−20	−02	−05	14	04	−22	02	−08	34
71	36	30	22	06	17	22	−03	−01	14	28	−08	21	−27	−06	08	02	00	−09	03	54
72	93	−12	−01	15	00	−03	00	06	48	−28	006	05	−10	−11	00	−34	03	39	03	64
73	42	−11	−19	11	24	−29	−10	−12	−09	08	−05	−14	27	15	−11	03	−13	13	66	80
74	94	01	−31	−00	09	−03	05	01	04	−29	−04	01	−06	−08	30	08	−17	50	−01	58
75	8	27	17	16	−03	16	−09	13	−04	−34	04	03	21	25	−03	−08	05	−06	−07	42
76	22 and 131	38	−04	05	08	−14	14	04	−10	−10	20	04	−04	−09	16	24	08	10	05	42
77	46 and 137	03	05	−29	34	−18	−00	−04	18	08	−40	−08	−05	−03	03	04	−01	01	−01	45
78	98	25	02	−12	−09	18	−10	09	−01	45	07	03	−26	−10	−30	01	−05	10	01	72
79	92	−01	−19	−07	−18	08	08	04	31	02	−07	−14	−07	−12	−04	01	−02	15	−01	27
80	43	−09	−08	−14	03	04	12	−14	15	09	−07	04	−13	−12	−11	12	00	−05	−07	18
81	113	07	−03	−11	−23	−02	−25	−21	−00	03	08	15	−04	−12	05	06	−12	−04	02	32
82	83	−02	−03	01	−36	−10	08	−06	−12	20	20	04	−05	10	−12	20	11	41	−05	48
83	161	03	−21	−12	34	20	−10	−21	06	24	02	06	11	−19	02	20	−02	08	−05	44
84	162	01	−08	−14	12	−10	−13	46	12	01	04	−09	−13	−04	−08	−15	−05	15	−19	47
85	163	00	−24	07	22	07	−13	14	15	−03	07	09	−02	−38	12	−01	−03	−08	10	31
86	164	12	−18	−25	−07	21	05	−01	16	02	−06	−08	06	31	−00	27	−05	−10	−02	38
87	165	−22	14	01	−27	31	−18	−02	01	−04	53	07	03	05	12	09	41	02	−09	72
88	166	40	−09	−31	−21	02	39	−13	−23	−23	03	10	25	12	09	−03	07	−35	04	72
89	150	−13	13	−36	−14	00	−10	−22	07	09	−13	23	−15	−57	−10	−05	00	02	−06	62
90	150*b* (196)	06	02	−09	−01	−16	−02	−20	−07	02	−17	05	−11	19	23	−12	07	01	−02	25
91	2 (i) (172)	−25	−01	−14	12	08	13	−13	−12	−03	−10	−20	22	−09	09	03	−14	−04	−22	33
92	2 (iv)	−69	13	05	04	18	−12	−20	01	−03	−07	−03	−11	−06	06	−07	−13	09	03	66
93	2 (ii) (173)	−17	12	−66	−12	02	23	−21	03	06	−20	−07	18	−21	−06	−19	−05	−03	09	68
94	2 (iii) (174)	−14	−03	−44	14	−03	23	−20	17	13	−30	23	15	−18	−08	−02	−09	07	−08	53
95	6 and 177	53	30	−28	−08	00	18	−17	13	06	06	−06	−13	13	06	23	−04	15	−04	74
96	120	−20	−03	17	05	06	08	−29	−50	−07	06	05	14	06	−15	−01	−20	−04	−08	54
97	167	48	02	−23	−22	−05	02	−01	07	−07	20	04	−09	−02	01	47	−10	−07	05	86
98	67*b* (141)	02	01	−36	−11	−07	−40	−42	−03	11	−16	14	07	−21	20	−09	−00	01	−10	83
99		07	−06	07	08	20	28	37	15	−09	−06	−21	−09	13	−01	02	−05	02	03	58
100	111 (i)	26	40	12	23	−03	−04	−02	−06	−05	09	37	02	−19	−08	−11	00	−11	−06	58
101	126	−20	09	01	−02	−05	−20	−01	−30	17	−33	−13	−14	−09	14	18	22	21	−08	51
102	62 (138)	19	04	01	−20	13	08	09	28	−10	22	01	−03	−05	−09	02	−03	−15	08	30
103	25*c* and 132	01	04	09	−19	32	−05	11	17	−08	53	14	05	−16	−11	−00	−12	−05	−02	54
104	3*b* (127)	48	32	−15	−15	−20	−02	10	−06	04	10	−05	−02	10	−05	14	−14	−04	12	73
Number in ± 10 hyperplane		46	56	51	48	60	51	52	58	62	58	63	47	63	60	64	63	71	68	

for One's Values ; Indecisiveness ; Pessimism over doing good ; Criticism of Obvious Remarks ; and Restraint in Judgment.

3. THE EXPERIMENT AND THE FACTOR ANALYSIS.

The above tests consist of an individual battery of 15 tests and a group battery of 61 tests. The latter was administered in four 2-hour sessions over two successive days. (Test periods were shorter and rest periods longer than for the normal group. Attendants removed one or two subjects who became unco-operative.) In the individual testing, lasting three hours, rest pauses and a change were given at the end of each hour and tests which were likely to put stress on the subject were left to the end of the period.

For comparability with the normal group having essentially the same battery (14), as well as for easy test procedure, the educational level was kept as high as was compatible with getting 100 subjects from four mental hospitals. Even so, it had to be set down to a mean education level of 11·5 years. Thus 5 had only an elementary school education ; 80 had high school education and 15 had been to a university. The group is thus educationally somewhat poorer than our average normal group (8, 9, 14, 15). The mean age was 26·9, with a sigma of 4·6 and a median of 28 years. Since most of our normal groups have been men this also was kept a male population.

Psychiatrically the group included 76 schizophrenics, 4 severe psychoneurotics, 1 manic, 12 unclassified and 7 psychopaths. Naturally, cases proving too disturbed for testing, in the trial run undivided testing, which was first in the series, were not included in the group testing ; nor did we include cases undergoing shock therapy at the time. Consequently we lost 25 cases as incomplete, leaving 100.

The statistical treatment may be summarized as follows : The raw scores were rescaled to a 19 point range and normalized at the same time. From these a correlation matrix was calculated (product moment) on the 64 most important variables and a multi-group factorization yielding fifteen factors was carried out. While the rotation was in process certain errors were discovered in the scoring formulae for eight tests. At the cost of two years' delay we scrapped the analysis and decided to begin again (with revised test scores) and with a matrix now of 104 tests. (Previously we had planned to bring in the extra 40 tests as a matrix extension after factorization ; but improvements in I.B.M. methods during this time encouraged us to try a 104 × 104 matrix with 5,356 correlation coefficients). The ruins of the first factorization provided us with one advantage : a knowledge of those groups to be used for the multi-group extraction which would yield factors roughly at the true rotation positions.

The final multi-group factorization now yielded approximately these factors, plus three others—18 in all. It was rotated for simple structure, with the help of the new Electronic Rotator, designed by Carroll and Gaylord, at the Personnel Research Section, Adjutant General's Office, Washington, D.C., which shortened the process by two months and for which the experimenters wish to express their gratitude. A definite structure was obtained after 18 rotations, but it is not quite as good, judged by percentage in hyperplanes, as in the normal groups.

To save printing costs the unrotated and the transformation matrices have been stored on microfilm and may be obtained for two dollars from the Library of Congress, Auxiliary Publication Section, on application. The rotated matrix is presented here in Table I and the angles among the reference vectors in Table II. It will be seen that the factors are for all practical purposes orthogonal, being notably less correlated than those in ratings and questionnaires.

TABLE II.—*C. Cosines of Angles Among Reference Vectors.*

actor.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
1 .	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
2 .	03	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
3 .	−16	−02	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
4 .	02	−10	06	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
5 .	07	11	07	−04	..	..	..	..	..	..	..	..	..	..	..	..	..	..
6 .	15	08	−31	−07	−20	..	..	..	..	..	..	..	..	..	..	..	..	..
7 .	−03	−09	16	−03	−01	−19	..	..	..	..	..	..	..	..	..	..	..	..
8 .	05	−11	−05	−08	03	00	−12	..	..	..	..	..	..	..	..	..	..	..
9 .	02	20	−33	−02	−07	00	08	00	..	..	..	..	..	..	..	..	..	..
10 .	−09	−07	15	−10	00	01	13	04	−01	..	..	..	..	..	..	..	..	..
11 .	08	−11	06	03	14	−05	−08	−01	−15	−06	..	..	..	..	..	..	..	..
12 .	07	06	−21	08	00	21	−01	−04	17	11	−12	..	..	..	..	..	..	..
13 .	−01	04	18	−08	05	06	02	−01	−01	01	−06	−06	..	..	..	..	..	..
14 .	10	01	−04	−01	13	−15	03	−02	−04	−03	05	−10	−05	..	..	..	..	..
15 .	−04	−10	02	−02	05	10	−02	−01	03	00	08	25	01	−03	..	..	..	..
16 .	10	05	04	−19	11	−06	05	10	14	01	05	−09	03	14	00	..	..	..
17 .	−02	−04	00	−03	−01	−01	−14	14	02	−03	02	−18	03	02	−03	07	..	..
18 .	13	01	02	01	−02	−11	−01	−01	−05	04	−04	20	−03	04	−15	08	−01	..

4. THE NATURE OF THE FACTORS.

Our attempt to get a first interpretation of the factors will, as usual, be based upon an examination of that selected 10 per cent. (or less) of the variables which are most highly loaded in each factor studied. At this juncture in research progress, with the simultaneous publication of four analyses on parallel batteries with normal subjects (8, 9, 14, 15), it would also be possible to enter on more discursive interpretation, involving detailed cross references to these other populations and factor findings. Both space limitations, and the desirability of independence in initial interpretations in each field, persuade us, however, to keep this discussion of wider interpretations and identifications at a minimum. The reader may rest assured that the meaning and use of these hard-won factor measures will not ultimately be left at the level of the restricted initial statement presented here, but will be developed in further articles (10).

In setting out of factors the usual course (8, 9, 14, 15) will be followed of putting the Matrix Number on the extreme left, followed by the Master Index, and then the loading on the extreme right. The title of the test will be corrected to " High " or " Low," etc., to agree with the sign of the loading. The cut-off point in proceedings to list variables of lower loading will be made at a natural break, as near as possible to the limit of 5 per cent. significance of loadings. In terms of original correlations this would fall here at about 0·13; but we have made our cuts at at least twice this figure. However, where a variable loads no factor at a very significant level it is included, in parenthesis, in the factor which it loads *most highly*.

Factor 1. *General Intelligence.*

Matrix Number.	Master Index.	Test.	Loading.
92	2 (iv)	Low Motor Rigidity. Test 2	−69
61	11*b* (130)	High Intelligence: Verbal and Numerical	57
28	148	Much Aspiration for Improvement (Coding)	−54
65	98 (143)	C.M.S. Many Decisions Correct	53
4	153	C.M.S. High Speed of Making Decisions	53
95	6 (177)	High Ideo-motor Speed	53
30	26	High Ability to Handle Surprises (Riddles)	50
97	167	High Efficiency of Immediate Memory	48
104	3*b* (127)	High Speed of General Judgment	48

This factor has all the characteristic markers—intelligence test, memory, speed of judgment, low rigidity—of the general ability factor. (Found in F6 in (1), F2 in (2), F3 in (3), F2 in (4), F8 in (5)). One particular rigidity measure has strayed unduly high, but the mean of four of them is about right. Typically this also has the poorest hyperplane (44 per cent.) of any factor, due to intelligence influencing so many facets of behaviour.

Factor 2. *Manic Tendency.*

Matrix Number.	Master Index.	Test.	Loading.
5	15	C.M.S. Unrestrained Use of Circles	·77
47	108	Much Self-Confidence in Untried Performances	·45
4	153	C.M.S. High Speed of Decision	41
63	124*b* (195)	Tendency to Disagree. 2	40
100	111 (i)	Much Self Reference in General Events	40
38	152	Tendency to Disagree. 1	−33
54	116	Much Cynicism or Hard-headed Judgment	33
19	96*a* (188)	Much Effect of Frustrated Pref. on Comp.-ut. Speed	32
104	3*b* (127)	High Speed of General Judgment	32
74	94	Low Mean Frequency of Flicker Fusion	−31

In the two rapid C.M.S. performances, the high confidence claimed and breadth of experience, and in high oscillation (not high enough, however, to be in the top eight) this factor closely resembles, though not necessarily enough for an unquestionable match, the earlier factors F10 in (3) and F13 in (6). The psychological consistency is very good and we shall hypothesize that this is a dimension of "manic tendency," governing rapid and rash action (Variables 4, 5, 104), egotism (Variables 38, 63 and 100), high self-confidence (Variables 47, 58), and resentment at minor frustration (Variables 19, 38, 63). This hypothesis will be checked in the ensuing breakdown of factor measures by syndrome groups.

Factor 3. *Stoicism.*

Matrix Number.	Master Index.	Test.	Loading.
93	2 (ii) (173)	Low Motor Rigidity. 5	−66
45	103 (ii) (192)	Little Considered Possible in Given Time for Self	44
94	2 (iii) (174)	Low Motor Rigidity. 6	−44
50	112	High Ratio Adverse to Favourable Self Reference in Events	38
89	150	Little Extremity of Viewpoint	−36
98	67*b* (141)	Little Extremity of Viewpoint	−36
88	166	Low Ratio of Normal to Shock Performance (Class.)	−31
7	43 (i)	Low Ratio of Reaction on Mental to Physical S. in P.G.R.	−31
60	99	High Ratio of Verbal to Numerical Ability	30

Although this factor is rotated to the best hyperplane we have been able to find, the pattern is puzzling, in two respects. First it resembles, in low rigidity and low ratio of normal to shock performance, the previously found series of factors F9 in (1), F11 in (2), F2 in (3), and F3(–) in (6), but so also does factor 13 below. Both lack the clear involvement with slow reaction times which these have. Secondly, it shares (when reversed), with factor 7 in the present series, a resemblance to Eysenck's (17) neuroticism factor. Factor 7 *has* the slow reaction times. Either Eysenck's factor is really two factors or else some new factor rotation has eventually to be found between the present 3 and 7. Contingently the term " Stoicism " perhaps best suggests its general character, for the person is little perturbed by shock, and takes a coldly realistic view of events.

Factor 4. *Novel Pattern No.* 1.

Matrix Number.	Master Index.	Variable Title.	Loading.
19	96 (*a*) (188)	Little Effect Frustr. Preference on Comp. Speed	−71
10	25	High Ratio Emotional to Non-Emotional Recall	40
11	115 (i) (193)	Ego Strength 1. Little Shift from Unsuccessfuls	−39
82	83	Low Fidgetometer Frequency	−36
77	46 (137)	Much Impairment Unseen Maze P. by Discomfort	34
83	161	High Ratio of Performance (Cancel.) Approval to Disapproval	34

This factor resembles no previously known pattern and justifies no discussion until confirmed in other populations.

Factor 5. *Insecure Contra-Suggestibility.*

Matrix Number.	Master Index.	Variable Title.	Loading.
63	124 (*b*) (195)	Tendency to Disagree (Ratio Score: Optimism-Pessimism Material)	−68
31	106	Little Unreflective Acceptance of Unqualified Statements	−61
38	152	Little Tendencv to Disagree (Diff. Score Largely Opt.-Pess. Material)	−39
68	38*b* (135)	Low Ratio Consonant to Dissonant Opinions Recalled	−39
18	31 (i)	Little Fluctuation of Attitudes. Material 4	−34
40	65*b*	Low Logical Consistency of Attitudes	−33
103	25*c* (132)	High Ratio of Emotionally Interesting to Emotionally Dry Recall	32
87	165	High Ratio of (Classification) Performance under Approval to Disapproval	31

The combination of " Disagreeing " with " Low ratio of recall of consonant to dissonant opinions " has been found before in F5(—) in (1), F6 in (4), F3(—) in (5) and F4 in (6), but has there had more emphasis than here on the attitude shift measures. (A pattern found here more clearly in Factor 7.) However, the loadings, though lower, are consonant, showing ego weakness (Variables 11, 13) and immaturity (Variable 15) associated with the present pattern. The whole strongly indicates a preoccupation with independence and relation to authority, together with a basic insecurity and suggestibility, such as occurs in extreme forms in schizophrenia.

Factor 6. *Cyclothymia* (*Reversed*).

Matrix Number.	Master Index.	Variable Title.	Loading.
14	31 (iii)	Low Fluctuation of Attitudes. Material 3	−62
12	31 (iv)	Low Fluctuation of Attitudes. Material 4	−58
16	31 (ii)	Low Fluctuation of Attitudes. Material 2	−57
98	67*b* (141)	Little Extremity of Viewpoint	−40
45	103 (ii) 192	High Amount Considered Possible in Given Time for Self	−40
88	166	High Ratio of Performance Normal to Shock	39
40	656	Low Logical Consistency of Attitudes	−25
81	113	Much Breakdown of Reality Principle	−25
69	41	Little Two Hand Co-ordination	−24

The pattern of low attitude fluctuation, little extremity of viewpoint, and breakdown of reality thinking (as opposed to pleasure principle) occurs, exactly as here, in previous factors F9 in (2) and F1 in (3). Earlier still (3) attitude fluctuation had been shown to be associated with cyclothymia and with general instability. Our hypothesis is that the present factor is the cyclothymia factor and Factor 7 the general instability factor, for 7 is the only other factor with systematic relationships to fluctuation measures. Since this population is selected for instability it is not surprising that here, in contrast to a normal population, the decidedly larger fraction of fluctuation variance falls in the cyclothymia factor.

Factor 7. *Emotional Stability* vs. *Neuroticism*.

Matrix Number.	Master Index.	Variable Title.	Loading.
84	162	High Ratio Perform. (Cancel.) Normal to Shock	46
48	114	Little Underestimation Pros. Perf. in Unex. Dif. Mat.	−43
98	67*b*	Little Extremity of Viewpoint. 1	−42
32	7	High Speed of Perceptual Closure	38
69	41	Good Two Hand Co-ordination	37
99	326	Low Ratio of Errors to Attempts	−36
27	28	High Dynamic Momentum	36
50	112	Low Ratio Adverse to Tav. Self Ref. in Events	−35
13	115 (ii) (194)	Ego Weakness. 2. Avoidance of Designated Neurotic's Response	32
96	120	High Ratio of Inaccuracy to Speed	29

It should be noted that the rigidity measures (Variables 91, 92, 93 and 94)—important markers in personality research—have systematic relations to four factors in this study: 3, 1, the present factor, and 10, in that descending order. The long history of research (2, 5, 11, 19, 20, 22) associating rigidity with emotional instability should not blind us to the possibility that its association with other personality factors *might* be still higher. Indeed, the studies from this laboratory have repeatedly (8, 9, 11, 14, 15) shown its variance to be distributed among four factors, one being intelligence (F1 here), one instability or neuroticisms (as in Eysenck's findings (17) and the two other being factors of which we are only just beginning to get a clear view (3 and 10 here).

Although Eysenck has made rigidity and sway suggestibility (or ataxia) central to measurement of the neuroticism factor as he defines it, we have consistently found these variables present but of low loading (as here), compared to other available tests, in the same factor as it appears in our rotations. From the present and other studies we are suggesting that a battery for the measurement of neuroticism should add to these two tests (with equal or greater weight), measures of Extremity of Viewpoint, Ratio of Inaccuracy to Speed, High Aspiration Level (except in unusually difficult material, as above), Inability to State Assumptions, Preference for Form over Colour (in Pictures), Slow Speed of Judgment, and Poor Two Hand Co-ordination. (As defined in the studies concerned.) The present factor indicates possibilities also for Low Dynamic Momentum, Slowness and Inaccuracy of Perceptual Closure, and Much Acceleration of Cancellation Performance by Electric Shock. The present factor can be matched with F10 in (1), F7 in (3) and F5(—) in (6).

Factor 8. *Inhibition by Social Standards.*

Matrix Number.	Master Index.	Variable Title.	Loading.
67	91	Little Artistic Suspicion	−53
96	120	Low Ratio Inaccuracy to Speed	−50
72	93	Little Effect of Restraint on Performance	48
49	105	Much Tendency to Perceive Threatening Objects	40
63	124*b* (195)	Tendency to Disagree. 2	−39
50	112	High Ratio Adverse to Favourable Self Ref. in Events	34
79	92	Slowness to Imitate Animal Sounds	31

This matches, notably on Seeing Threatening Objects, Tendency to Disagree, Good Knowledge of Social Etiquette, Large Mean P.G.R. Response and Much Impairment of Maze Performance by Shock, the previously matched F2 in (1), F4 in (2), F11 in (3) and F14 in (6). However, the two last variables, and Absence of Questionable Preferences, also agree in pattern with the present factors 12 and 16. The total pattern and its meaning, nevertheless fits best here, as a factor of inhibition and diffidence, combined with high social and general standards and a tendency to suppressed hostility. Our hypothesis is that this corresponds to an acquired general inhibition derived from a more exacting social environment.

Factor 9. *Novel Pattern No.* 2.

Matrix Number.	Master Index.	Variable Title.	Loading.
78	98	C.M.S. Many Decisions Correct (R–W)	45
65	143 (98)	C.M.S. Large Absolute No. Decisions Correct	45
51	109	Low Ratio of Pleasant to Unpleasant Associations	−38
25	30 (134)	Low Ratio Criticism of Self to Criticism of Others	−35
50	112	Low Ratio of Adverse to Favourable Self-Reference in Events	−35
75	8	Low Rate of Alternating (Cube) Perspective	−34
54	116	Marked Cynicism or Hard Headed Judgment	33
39	97	Time Interval Perceived Longer During Work	30
74	94	Low Mean Frequency of Flicker Fusion	29

No *single loading* is high enough here to give a clear lead on the meaning of the factor, and since the *pattern* has not been previously encountered it would seem best to await its confirmation in later studies.

Factor 10. *Novel Pattern No.* 3. *Sensitive Self Regard.*

Matrix Number.	Master Index.	Variable Title.	Loading.
87	165	High Ratio of Performance (Classif.) Under Approval to Disapproval	53
103	25*c* (132)	High Ratio of Emotionally Interesting to Emotionally Dry Recall	53
45	103 (ii) (195)	Much Considered Possible in Given Time for Self	−45
77	46 (137)	Little Impairment Unseen Maze Performance by Discomfort	−40
27	28	High Dynamic Momentum	39
28	148	Little Aspiration for Improvement	34
94	2 (iii) (174)	Low Motor Rigidity. Test 6	−30
50	112	High Ratio Adverse to Favourable Self Reference in Events	28

The person high in this factor is not upset by difficulties or discomforts and shows good control, as evidenced by low rigidity (which follows through in the remaining rigidity tests), but he is deterred by disapproval, takes a realistic or pessimistic view of how things will affect him and does not set an unrealistically high aspiration level.

The pattern suggests the sensitive but tenacious outlook of the schizothyme factor A — , found in ratings.

Factor 11. *Socialized Maturity.*

Matrix Number.	Master Index.	Variable Title.	Loading.
39	97	Time Interval Not Perceived Longer During Work	−52
54	116	Lack of Cynicism in Judgment	−47
21	155	Small Range of Flicker Fusion	−39
100	111 (i)	Much Self Reference in General Events	38
38	152	Tendency to Agree. 1	36
17	35	Little Suggestibility to Authority	−35
45	103 (ii) 192	Low Amount Considered Possible in Given Time for S.	28
57	107	Good Knowledge of Etiquette	28

In variables 39, 38, 17 and 45, as shown, this factor resembles F5(—) in (4), F11(—) in (5) and F8(—) in (6), and it does so also in the lower, but out-of-hyperplane loadings for low speed of perceptual closure, low estimate of time required for tasks by others, little extremity of viewpoint, and little shift toward successfuls, i.e., ego strength. But the match is not really good on account of sign inconsistencies.

The pattern shows both maturity, e.g., in time estimate, insuggestibility, etc., and a marked awareness of social relations (Variables 54, 100, 57) and is therefore perhaps best described by the given label.

Factor 12. *Novel Pattern No.* 4 : *Nervous Exhaustion.*

Matrix Number.	Master Index.	Variable Title.	Loading.
24	4 (176)	Long Mean Reaction Time ; Irregular signals	57
23	4 (175)	,, ,, ,, ,, Regular ,,	53
59	2	High Perceptual Rigidity ; Hidden Words	−52
45	103 (ii) (192)	Much Considered Possible in Given Time, for Self	−50
30	26	Little Ability to Handle Surprises. Riddles	−49
57	107	Poor Knowledge of Etiquette	−47
18	31 (i)	High Fluctuation of Attitudes. Material 1	44
16	31 (ii)	High Fluctuation of Attitudes. Material 2	43

This factor may represent a fatigue state rather than a more permanent personality dimension. There is a consistent lack of alertness and of capacity to cope with unusual situation (Riddles, Perceptual Rigidity) as well as a marked fluctuation of attitude, which is also characteristic of central fatigue. This pattern would repay study as a basis for the measurement of nervous exhaustion.

Factor 13. *Novel Pattern No.* 5 : *Surgency* v. *Desurgency.*

Matrix Number.	Master Index.	Variable Title.	Loading.
1	157	Many Jokes Overtly Reacted to as Funny	54
89	150	Little Extremity of Viewpoint. Material 2	−54
26	156	Little Lag of Flicker Fusion	−40
21	155	Little Range of Flicker Fusion Speeds	−39
85	163	Low Ratio of Performance (Perceptual Closure) under Approval to Disapproval	−36
44	13	High Oscillation	35
86	164	Low Ratio of Performance (Perceptual Closure) Normal to Shock	−32
53	29 (133)	Low Criticalness (Severity) of Judgment	−26

In the imperviousness to shock and disapproval, as well as in the oscillation, criticalness and humour this resembles the already matched set F9 in (1), F11 in (2), F2 in (3) and F3(—) in (6) which have been stated above to have a rival resemblance to the present Factor 3. Further examination must solve this point, but meanwhile the present factor clearly represents a pattern of happy-go-lucky attitudes and disregard for punishment suggesting the surgency-desurgency factor found in ratings (2, 5, 6, 7). Why precision of awareness of flicker fusion thresholds should associate with surgency cannot be answered at present.

Factor 14. *Novel Pattern No.* 6.

Matrix Number.	Master Index.	Variable Title.	Loading.
51	112	Low Ratio of Pleasant to Unpleasant Associations	−45
21	155	Large Range of Flicker Fusion Speeds	44
50	112	Low Ratio of Adverse to Favourable Self Reference in Events	−38
27	28	High Dynamic Momentum	37
65	98 (143)	C.M.S. Few Decisions Correct	−37
52	110	Low Anteversion-Retroversion Association Ratio	−33
74	94	High Mean Frequency of Flicker Fusion	31
78	98	C.M.S. Few Decisions Correct (R — W)	−31

It happens that few of the variables coming together here have been used in any one previous study, so a match is in any case unlikely. There is an intriguing relationship in that though the rational, conscious outlook tends to more favorable than adverse conclusions, the "free association" gives more unpleasant than pleasant associations and the individual looks to the past rather than the future. Together with the plodding concentration of Variable 27, this perhaps suggests a punishing super-ego and melancholic trends—an hypothesis that can be taken up in the syndrome analyses.

Factor 15. *Decisiveness.*

Matrix Number.	Master Index.	Variable Title.	Loading.
15	34	Maturity of Opinion	−61
97	167	High Efficiency of Immediate Memory	46
44	13	High Oscillation	40
17	35	Little Suggestibility to Authority	−33
72	93	Marked Effect of Restraint on Performance	−31
29	147	Small Estimated Breadth of Experience and Accomplishments	−27
32	7	Low Speed of Perceptual Closure	−25
76	22 (131)	High Ratio of Chance to Purposeful Observation*	24

* Highest loading here except in intelligence factor, where it is reversed.

This factor can readily be matched—by the combination of high maturity, low authority suggestibility, good memory, high speed of judgment (only 0·12 here, however), low speed of perceptual closure, and modesty of self appraisal—with a pattern which has manifested itself through six distinct researches (F8 in (1), F7 in (2), F4 in (3), F3 in (4), F1 in (5) and F10(—) in (6).

It is temporarily labelled "Decisiveness," but the other studies indicate decided physiological associations which require a search for an underlying explanation in temperament.

Factor 16. *Masculinity* v. *Femininity.*

Matrix Number.	Master Index.	Variable Title.	Loading.
55	117	Lack of Fashionable Good Taste in Social Matters	−49
87	165	High Ratio of Performance (Classification) Under Approval to Disapproval	41
60	99	Low Ratio of Verbal to Numerical Primary Ability	−35
10	25	Low Ratio of Emotional to Non-Emotional Recall	−25
3	158	Little Increase of Tempo under Threat	−25
25	30 (134)	Low Ratio Criticism of Self to Criticism of Others	−24
68	38*b*	Low Ratio of Consonant to Dissonant Opinions Recalled	−24
70	21	Pressure of Questionable Preferences	−24

The recording has been pursued to lower and less significant loadings than usual, largely because (except for 10, 25 and 68) the latter happen to be practically the highest loadings anywhere for the given variables. There is also some doubt on this factor's rotation because random variable 42 has a substantial loading on it. (Only on Factors 11 and 13 do the random variables otherwise exceed loadings of 23). However, the pattern is a tolerable match for F3(—) in (1), F1(—) in (2), F10(—) in (4), and F12(—) in (5), combining lack of highbrow taste, low criticism, questionable reading preferences, few C.M.S. errors and low ratio of consonant to dissonant opinions. This factor has such an appreciable correlation with sex difference that it has been called previously "Masculinity–Femininity" (14) and to this we adhere in the present title.

Factor 17. *Novel Pattern No.* 7.

Matrix Number.	Master Index.	Variable Title.	Loading.
74	94	High Mean Frequency of Flicker Fusion	51
72	93	Little Effect of Restraint on Performance	41
82	83	High Fidgetometer Frequency	41
22	5	High Ratio Reg. to Irreg. Warned Reaction Time	38
66	95	Much Myokinetic Movement Decrease under Threat	37
21	155	Large Range of Flicker Fusion	35
88	166	Low Ratio Performance (Class) Normal to Shock	−33
35	151	Shorter Time for Decision Principle than Partic.	−32

Though resemblances are noticeable in past findings none is clear enough for a match, and the pattern is best left as novel ; with the comment only that it suggests a generally " high strung," tense, concentrated person, as quick on unwarned as warned reaction time and whose concentration is not reduced by shock.

Factor 18. *Novel Pattern No.* 8.

Matrix Number.	Master Index.	Variable Title.	Loading.
73	42	High Body Sway Suggestibility	66
7	43 (i)	Low Ratio Mental to Physical Stim. React. on P.G.R.	−39
64	122	High Static Ataxia (Simple Body Sway)	35
1	157	Few Jokes overtly Reacted to as Funny	−29
62	101	Lack of Excess of Aspiration Level over Performance (Coding)	−28
37	125	High Ratio of Personal to Institutional Values	25
49	105	Little Tendency to Perceive Threatening Objects	−25
46	119	Lack of Artistic Taste in Colour Blending	−22

This factor of smallest variance has appreciable loadings only in the sway tests and in reacting more to physical than mental threats. It has not been found in other populations and does not justify discussion until confirmed.

5. SUMMARY.

(1) One hundred and two objective personality measures (from 76 tests), devised in relation to hypotheses already emerging from several personality factor studies, were administered to 100 adult male psychotics. The test battery, consisting of group and individual tests, was designed also to have about 80 per cent. overlap of measures with those used on normal adult groups in six other researches.

(2) Intercorrelation and factor analysis (rotated to simple structure) yielded eighteen factors, ten of which could be contingently matched, in terms of common variables having similar patterns of loadings, with factors found in the other studies.

(3) An initial interpretation has been attempted for these ten factors, but the remaining eight are simply recorded, waiting to be confirmed or modified by other researches.

(4) The conclusion may be drawn that the majority of personality dimensions in objective tests are the same for psychotics as for normals, though the follow-up research on absolute levels may show that they are possessed in very different degrees.

(5) As far as applied psychology is concerned the way has been prepared for constructing personality factor measures of greater factor saturation than those employed in this exploratory study. For now that initial batteries are available to distinguish each factor, new, lengthened tests can be simply validated by " item analysis " against any one factor pool, without the necessity for experimenting with a hundred or more tests, or for the more complex processes of rotated factor analysis.

The above tables should suffice for researchers wishing to construct test batteries for individual factors. However, for greater comparability they may perhaps better use the mimeographed, twelve-factor battery which is currently being prepared for distribution by the Institute for Personality aud Ability Testing, 1608, Coronado Drive, Champaign, Ill., U.S.A. This initial standard battery of objective personality tests is put forward now in the hope that interested researchers may (1) seek by " item analysis " (including use of new test designs) to arrive at more saturated measures, and (2) test the predictive value of the factor measures, i.e., their social validation, in terms of diagnosis and prognosis, and their value in plotting changes occurring under therapy.

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A STUDY OF INDIVIDUAL DIFFERENCES AND OF INTERACTION IN THE BEHAVIOUR OF SOME ASPECTS OF LANGUAGE IN INTERVIEWS.

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I. Introduction.

Since the interviewing process, or the process of two people talking to each other is an extremely complex phenomenon, it seemed advisable to begin its analysis at the elementary and quantitative level, by first of all measuring the duration both of periods of continuous speech, and of the pauses and then after investigating their various relations and rhythmic alternation, to work up through grammatical analysis to the more complex phenomena.

II. Experiment.

An experiment was staged in which three senior psychiatrists of Maudsley Hospital (who will be referred to as D1, D2, and D3), took part. They were chosen on the basis of a judged difference in their conversational activity, the experimenter predicting essentially different scores for D1 on the one hand

and D2 and D3 on the other. A group of patients, five reserved (four cases of depression and one of uncertain diagnosis), and five talkative (four cases of anxiety and one uncertain), were then selected to be interviewed by all the three doctors in rotation. There were thus 30 interviews altogether. Any errors arising from the order of interviewing, that is, from the fact that patients would respond differently according to whether they were interviewed for the first, second, or third time, irrespective of which doctor interviewed them, were controlled by putting them in random order.

The three interviewers were thus compared against a constant stimulus background. Furthermore, in order to make the interviews comparable a common aim was set, namely to describe and diagnose the patients' present mental state. The doctors were, within those limits, given freedom to use their own personal technique and approach.

These interviews were recorded both on the interaction chronograph, giving a continuous record of the length of time taken up in action (speech and relevant gesture) and silence by each of the speakers, and also on the speech recorder.

III. Previous Results.

The following results, reported elsewhere in detail (4), emerged from the analysis of the time recording (interaction chronograph).

1. Interviewers showed themselves to behave consistently, irrespective of the type of patient interviewed, with respect to two of the three measures taken: (*a*) bs/ds, i.e., the ratio of the total number of short silences (bs) to the total number of long silences (ds) in the speech of the interviewer, and (*b*) A + S, i.e., the average period comprising an action (A) plus its subsequent silence period (S). As regards the third measure used, namely AT, i.e., the total amount of time that was spent in action (talk and gesture) expressed as a percentage of the total time of the interview, the interviewers showed themselves consistent in relation to each other, but all adjusted themselves to about the same extent when passing from the reticent group of patients to the talkative.

The patients' conversational behaviour was consistent with respect to bs/ds, and AT. While the latter value, i.e., the amount of time spent in talking, proved independent of the interviewers, the bs/ds score (activity rate) showed itself sensitive according as one or the other doctor was the interviewer. A + S (conversational tempo) did not show reliability but seemed subject to interviewers' influence.

In short, the interviewers showed themselves more rigid with respect to activity rate (bs/ds) and tempo or rhythm of interaction while being highly flexible with respect to the amount of time they talked in an interview. Patients were most rigid with respect to the amount of time and activity, and seemed subject to influence in respect of tempo or rhythm of interaction.

IV. Grammatical Analysis.

The following results emerged from the analysis of the data obtained from the speech recorder. The records were transcribed to manuscript form and a count was then taken of all the words used by each of the speakers for the following grammatical categories: nouns, verbs, adjectives, and self-reference terms.

For each speaker, calculations were made of the average number of words spoken per minute (the "word rate"), and of the proportion of words in each of the selected grammatical categories to the total number of words uttered.

Unfortunately some of the speech recordings were fragmentary. In particular the subdued tones of the depressed patients presented the microphone with too difficult a task. Consequently only twenty-five complete records became available in the case of the patients. Among the doctors, eight of these recordings involved D1 as interlocutor, seven D2, and ten D3.

The question was then asked whether any of these facets of language behaviour could be shown to be consistent for individuals. For the doctors there were ten or at least seven to eight sets of figures available for each category, each doctor having conducted ten interviews. For the patients only three sets of figures were available each having been interviewed three times.* These figures are averages based on each interview as a whole summarizing language behaviour during stretches containing an average of about 2,300 words apiece.

An analysis of variance was computed for each of the above quoted grammatical categories, and also for the verb/adjective and noun/self-reference ratios, and the word rate, separately for doctors and patients.

1. *General Results.*

Tables I and II present an overall picture resulting from the analyses of the variance of the various categories of the language used in the interviews which are enumerated above.

Table I shows that, as far as the doctors are concerned, the word rate (number of words a minute), the percentage of self-reference terms, and the

TABLE I.—*Doctors.*

		Means.	S.E.	F-ratio.	P.	
Number of words per minute	D1	198·2	7·81	..	..	
	D2	168·1	4·28	10·6	·001	
	D3	222·7	9·73	..	..	
Self-reference terms, per cent.	D1	1·80	0·32	22·2	..	
	D2	1·66	0·21	..	·001	(F = 9·6)
	D3	3·93	0·28	..	..	
Nouns	D1	12·79	0·21	4·89	..	
	D2	10·60	0·54	4·89	·05	(F = 3·4)
	D3	11·18	0·60	..	·01	(F = 5·7)
Nouns/Self-reference terms ratio	D1	8·19	0·94	..	..	
	D2	7·36	1·43	10·8	·001	
	D3	2·98	0·30	..	..	
Adjectives	D1	8·27	0·67	..	..	
	D2	10·05	0·61	3·4	·05	
	D3	8·48	0·26	..	..	
Verb/Adjective ratio	D1	3·05	0·29	5·6	·01	
	D2	2·13	0·22	..	·01	
	D3	2·49	0·08	..	..	

---

* Complete records of three interviews each were available only for five patients.

TABLE II.—*Patients.*

		Means.	F-ratio (comparing interviews with D1, D2, D3).	P.	F-ratio (comparing interviews with D1 and D2 only).	P.	
Number of words per minute	P4	167·2					
	P6	187·5					
	P7	192·9	1·7	N.S.	69·5	·001	(F = 3·1)
	P8	214·1					
	P9	192·2					
Self-reference terms	P4	12·32					
	P6	11·10					
	P7	9·54	2·6	N.S.	76·1	·001	(F = 53·4)
	P8	10·14					
	P9	10·14					
Nouns	P4	14·16					
	P6	11·37					
	P7	14·41	1·36	N.S.			
	P8	11·40					
	P9	13·44					
Noun/Self-reference ratio	P4	1·15					
	P6	1·04					
	P7	1·61	1·67	N.S.			
	P8	1·13					
	P9	1·33					
Adjectives	P4	9·57					
	P6	9·99					
	P7	11·98	2·24	N.S.			
	P8	10·95					
	P9	12·06					
Verb/adjective ratio	P4	2·40					
	P6	2·06					
	P7	1·49	4·19	·05	(F = 3·8)		
	P8	1·78					
	P9	1·46					

ratio of nouns to self-reference terms, have all proved highly reliable categories of language, discriminating between the three doctors significantly with a probability of ·001.

The verb-adjective ratio, the percentages of nouns and of adjectives are also consistent with a lower reliability (P = ·05), the verb-adjective ratio being the most constant among these measures.

As to the patients, whose tests are summarized in Table II, only the verb/adjective ratio discriminates significantly (P = ·05) between the individual patients when the scores from their interviews with all three doctors are compared. On inspection of the figures, however, it can be seen that for the word rate (number of words a minute) (see Table III) and the self-reference percentages (see Table IV) there was little variation in the scores obtained from the interviews with D1, and D2, but that in the interviews with D3 their values shifted considerably. These shifts, however, did not occur consistently in one direction, D3 apparently having a different effect upon each patient. But they had this in common, that they were rather spectacular in comparison

TABLE III.—*Number of Words per minute for each Patient P4, P6, P7, P8, P9 given for each Interview.*

Doctor Interviewing.	P4.	P6.	P7.	P8.	P9.
1	157·4	184·1	175·5	217·6	193·5
2	177·4	183·7	170·7	215·1	188·5
3	166·7	194·6	232·5	209·6	194·7
Mean	167·2	187·5	192·9	214·1	192·2
S.D.	7·5	3·6	32·5	3·3	4·5

TABLE IV.—*Percentages of Self-reference Terms for Patients P4, P6, P7, P8, P9 given for each Interview.*

Doctor Interviewing.	P4.	P6.	P7.	P8.	P9.
1	11·99	11·12	10·78	9·29	9·23
2	12·29	11·71	10·82	9·99	9·56
3	12·69	10·46	7·02	11·14	11·62
Mean	12·32	11·10	9·54	10·14	10·14
S.D.	0·41	0·43	1·78	0·76	1·03

with the consistency of word rate and self-reference percentage maintained by the patients when talking to D1 and D2. Indeed, the consistency of word rate and self-reference terms, when based on the interviews with D1 and D2, proved to be very high, the correlations being 0·984 (P = ·001) and 0·986 (P = ·001). In conjunction with the fact that word rate and self-reference percentage had also been shown to be relatively invariant characteristics of the doctors' speech, it seems reasonable to assume that a considerable degree of constancy attaches to these two categories in the language of individuals generally*. The interviews with D3 seem, however, to have involved stimulation different in kind from that at work in the interviews with D1 and D2, with an ensuing different level of adaptation in these linguistic modes of behaviour.

To throw more light upon this phenomenon a further analysis was undertaken.

2. *Individual Differences between Interviewers and their Effect on the Patients' Responses.*

On examining the figures in the various categories for the doctors we can see that D3 had by far the highest rate of word output (222·7 words a minute as against 198·2 for D1, and 168·1 for D2) (See Table V), and the highest proportion of self-reference terms (3·93 as against 1·80 for D1, and 1·66 for D2) (see Table VI). It will be recalled that with respect to the time measurements reported previously (4), D3 proved to be the interviewer with the highest rate

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* However there was a difference in the scope of their constant behaviour as a comparison of the readings for word rate and self-reference percentage in Tables I and II will show. Word rate discriminates between individuals, but it is unaffected by their rôle in the interview, i.e., whether they are doctor or patient. The self-reference percentages, on the other hand, are quite different for the two groups, the patients' frequency of referring to themselves ranging about a mean of 10·7 per hundred words and the doctors' about 2·5. This difference is obviously related to the type of material produced by patients whose rôle it is to talk about themsleves. Word rate shows no such dependence and wide shifts in this form of linguistic action might possibly be manifestations of reactions at a deeper level.

TABLE V.—*Number of Words per minute for D1, D2, D3 given for each Interview.*

Patients interviewed.	Total number of words.		
	D1.	D2.	D3.
P1	..	..	223·0
P2	..	..	224·6
P3	202·3	180·7	237·1
P4	180·0	145·5	241·2
P5	237·1	—	262·3
P6	203·2	170·3	237·2
P7	214·5	167·6	236·4
P8	164·7	176·4	148·5
P9	198·8	160·0	211·6
P10	184·9	175·9	205·3
Mean	198·2	168·1	222·7
S.E.	7·81	4·28	9·73

TABLE VI.—*Percentages of Self-reference Terms for D1, D2, D3 given for each Interview.*

Patients. interviewed.	D1.	D2.	D3.
1	..	..	3·00
2	..	..	3·37
3	1·55	1·68	3·44
4	1·79	1·65	5·77
5	1·40	..	4·07
6	1·81	1·64	3·72
7	3·99	2·54	3·23
8	1·07	1·41	5·05
9	1·18	1·82	3·48
10	1·58	1·89	4·22
Mean	1·80	1·66	3·93
S.E.	0·32	0·21	0·28

of activity as measured by the ratio of short to long silences (bs/ds), and the fastest rhythm or tempo of interaction as measured by the average duration of each spell of activity and its subsequent period of silence (A + S).

On examining the individual figures for the patients' rate of word production and their proportion of self-references (it is in these two categories that D3 differs most strikingly from the other psychiatrists) it will be seen that P6, P7, and P8 were the ones whose interaction with D3 produced the most strikingly different values when the latter are compared with those obtained from their interaction with both D1 and D2. In the case of P6, and even more so in that of P7, this difference was very marked in the direction of speeding up their word production rate and reducing the number of self-references, whereas P8 on the contrary, spoke more slowly, and referred to the self more frequently when interviewed by D3 instead of by one of the other two psychiatrists. P7 offers the most extreme example, and a detailed study was undertaken of the deviation of this patient's language from that displayed in the course of being interviewed by D1 and D2. His behaviour was contrasted with that of P8 by assembling the essential information on these cases as far as it had emerged from this experiment. This analysis should lead to a better understanding of the background of interaction between P7 and D3, against which these changes occurred.

3. *The Interrelation of some Categories of Language Behaviour and their Psychological Significance.*

Considering the wide concurrent changes in word rate and self-reference percentage, the possibility of a functional relationship between these two measures demanded attention.

Estimating a mean level of word rate and of self-reference percentages on the basis of the patients' interviews with D1 and D2 (which would, of course, only be appertaining to interviewing situations having a comparable stimulation level), the relative positions of their deviations from it, in the interview with D3 were plotted, and it can be seen from Diagram I that for the five patients whose measures we have used in the analysis of variance a negative and possibly linear relationship seems suggested. In other words, a reduction of self-reference terms under the influence of D3 seemed to be accompanied by a speed-up in word production.

A further relationship suggested itself when it was noted that in the case of P7 there was not only a radical rise in word rate when talking to D3, and a concurrent drop in the self-reference percentage, but also a reduction in the total amount of speaking time, the proportions to the total interviewing time being 88 per cent. when talking to D1, 71 per cent. to D2, and 61 per cent. to D3. Plotting the deviations of the patients' total speaking time (AT) in the interview with D3 from their mean AT against their deviations of word rate from their mean word rate with D1 and D2, we again obtain what appears to be a negative linear relation (we would of course need more data to fit a regression line). In other words, a reduction in the amount of speaking time was in these cases accompanied by an increase in the word rate (number of words a minute or speed of talking). (Later observations (5) amply corroborate this relationship).

The relation of the AT percentage and of self-reference terms for the five patients in question was also plotted and Diagram I shows that (as would follow from the above) the correlation is positive.

Thus there is apparently a three-way relationship between these categories of language behaviour ; the percentage of self-references which these patients used in their interviews, the relative amount of total time taken up by the interviews during which they talked, and the rate at which they uttered words. While the proportion of self-references and of the amount of speech during the interviews changed in the same direction, the one increasing concurrently with the other, the word rate changed inversely, speeding up the less the patient spoke, and also the less he spoke about himself.

How much a patient actually does talk about himself is—at least partly—a function of the doctor's questioning. The decrease in the total amount of the talking time and increase in word rate or speed of talking would seem, on the other hand, to be aspects of adjustment to the interviewing situation. To return to the most extreme example of this, namely P7, it may be well to note

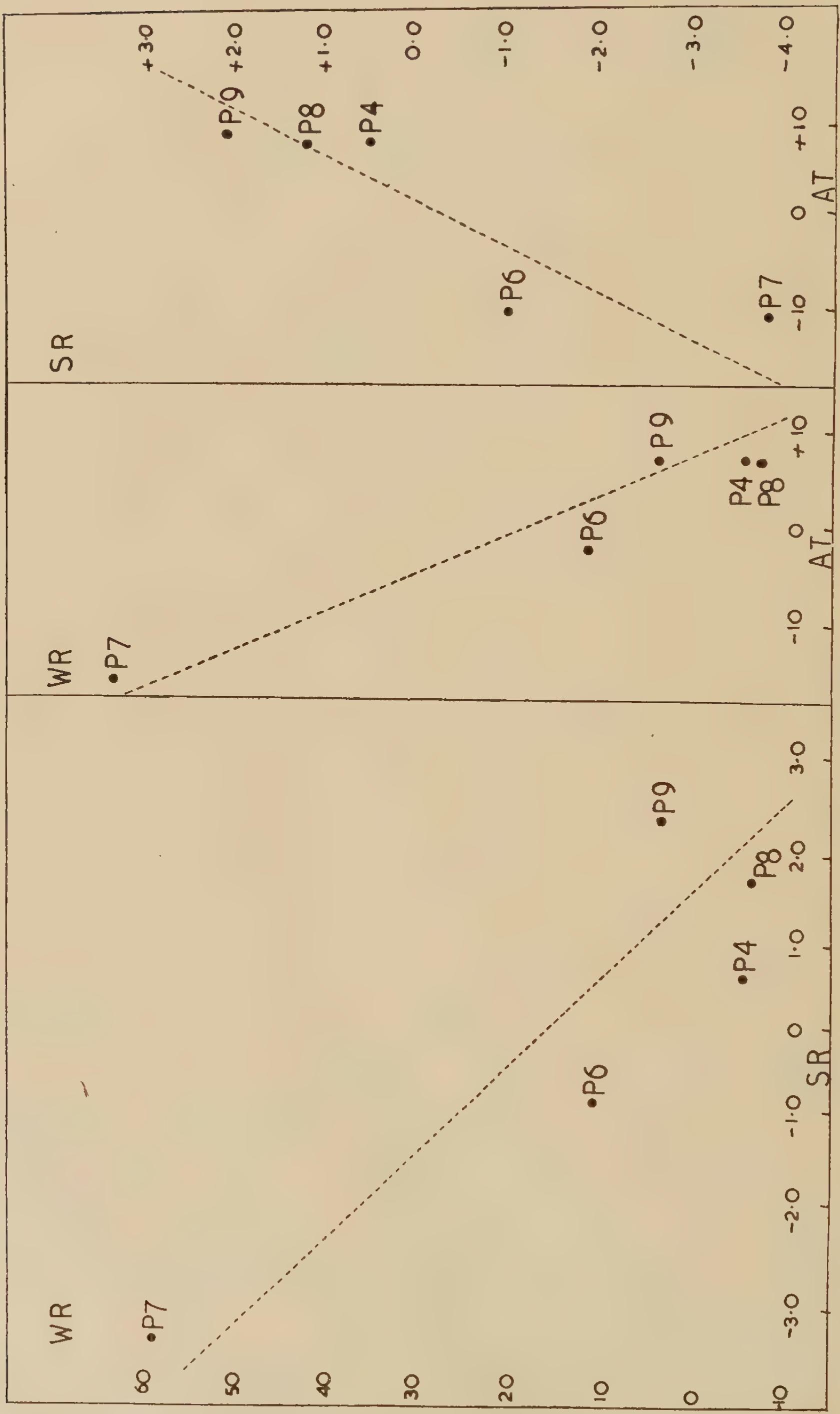

Diagram I.—Shifts of word rate and self-reference terms due to influence of D3 on P4, P6, P7, P8, P9. Shifts of word rate and action time. Shifts of self-reference terms and action time.

that in his interview with D3, his conversation also included a considerably longer period of mutual silence than his interviews with either D1 or D2. He sometimes failed to respond, while at other times he responded hurriedly as if under pressure. In the case of P8, we have the reverse picture, namely a higher than usual self-reference proportion, with a rise in the total amount of speaking time, and a slowing down in the word rate. That is, the patient talks in this interview more about himself than in the interviews with the other two doctors ; he seems under no pressure of acute time consciousness, and acts like somebody who has plenty of time to spare and can therefore afford to slow down. Acceleration in speech rate as intertwined in these two cases may thus turn out to indicate that the speaker feels under some kind of pressure, external or internal.

Corroboration for this interpretation was sought (*a*) by means of analysis of the content and (*b*) by contrasting both the changes in the language behaviour of D3 in the two cases of P7 and P8, and also the changes in the language behaviour of these patients themselves.

V. CONTENT ANALYSIS.

1. *Topic Analysis.*

These interviews having the purpose of coming to a diagnostic assessment had (with all the individual differences among the doctors) this in common, namely that the interviewer focused the attention of the patient on the subject about which he sought information. There were, of course, variations in the degree of initiative taken by the interviewer, but by and large the topics discussed were determined by the kind of questions put by the doctor. Table VII shows the percentage of the total number of words in each interview devoted to the various topics for each doctor and for each of the patients whose manuscripts in all three interviews were complete, i.e., P4, P6, P7, P8 and P9.

TABLE VII.—*Word Output expended by Patients P4, P6, P7, P8, P9 on Topics raised in Interviews with D1, D2, D3 expressed as Percentages on Total Number of Words used by the Patients.*

		Doctors.		
Topics.	Patient.	D1.	D2.	D3.
1. History of illness, mental state, early history etc.	P4	67·2	41·4	4·7
	P6	70·3	93·2	73·2
	P7	38·0	59·4	19·2
	P8	48·2	61·9	80·2
	P9	61·3	53·7	44·2
2. Family, domestic life	P4	..	1·5	7·8
	P6	..	1·5	..
	P7	..	..	7·1
	P8	1·6	..	..
	P9	..	5·0	..
3. Parents	P4	..	..	..
	P6	..	..	..
	P7	..	..	..
	P8	22·0	16·9	..
	P9	..	..	..

TABLE VII—*cont.*

		Doctors.		
Topics.	Patient.	D1.	D2.	D3.
4. Women, relationship with spouse	P4	..	17·5	..
	P6	..	..	..
	P7	..	..	..
	P8	7·9	7·5	..
	P9	..	1·4	..
5. Work	P4	..	..	..
	P6	..	..	..
	P7	19·2	6·9	23·0
	P8	10·1	10·3	10·0
	P9	..	10·4	6·8
6. Interests, outside activities	P4	..	..	8·2
	P6	18·6	..	..
	P7	11·0	..	8·4
	P8	2·7	1·8	..
	P9	7·0	8·9	21·4
7. Incidents, objective conditions, people, hospital	P4	..	..	..
	P6	8·9	..	22·6
	P7	6·3	8·7	..
	P8	..	..	..
	P9	7·6	..	..
8. Physical state, medical history	P4	7·9	..	4·4
	P6	..	..	..
	P7	7·1	..	..
	P8	..	..	..
	P9	7·3	..	19·6
9. Treatment	P4	..	3·7	29·4
	P6	..	..	..
	P7	5·8	..	..
	P8	..	..	..
	P9	..	20·0	..
10. Information	P4	..	..	4·3
	P6	..	..	..
	P7	3·3	..	12·2
	P8	..	..	..
	P9	..	..	..
11. Orientation	P4	22·8	..	..
	P6	..	..	..
	P7	..	..	..
	P8	..	..	..
	P9	..	..	..
12. Rapport	P4	1·9	1·6	..
	P6	2·7	0·4	1·1
	P7	1·1	0·8	8·2
	P8	0·4	0·2	0·2
	P9	0·7	0·9	1·9
13. Conclusion	P4	..	0·1	2·8
	P6	0·5	..	..
	P7	1·6	0·2	..
	P8	1·1	..	4·0
	P9	..	0·7	..
14. Miscellaneous	P4	..	..	..
	P6	..	..	..
	P7	1·7	..	..
	P8	4·0	..	5·0
	P9	..	..	..

From Table VII it can be seen that in all cases but two the bulk of the conversation centres on the subject of mental illness and condition of the patient. Here again the interviews with D3 show a different picture from those with D1 and D2. When interviewed by D3, less than one-quarter of all the words spoken by either P4 or P7 were concerned with this subject (19·2 per cent. and 4·7 per cent.), while when interviewed by D1 and D2, 67·2 per cent. and 41·4 per cent. respectively of all words uttered by P4 were on this subject. In the case of P7's interviews with D1 and D2 the corresponding percentages were 38·0 per cent. and 59·4 per cent. respectively. From this it appears that D1 and D2 were pursuing the standard routine procedure, while D3 seemed to have varied his procedure with the individual patient.

It is particularly interesting to note the wide discrepancy in the word output concerning the subject of mental state in the interviews which D3 conducted, and especially the wide discrepancy between P7 and P8, bearing in mind that in their language behaviour with D3 other discrepancies have already been noted. It can be seen from Table VII that only 19·2 per cent. of words spoken by P7 were about his mental illness and condition, whereas 80·2 per cent. of P8's total word output referred to the subject.

VI. THE ANALYSIS OF INDIVIDUAL DISCREPANCIES.

1. *P7 and P8 interviewed by D3.*

If we set out the divergencies from their means in the speech behaviour of these two patients side by side with D3's deviations from his own mean when interviewing them, the mean of D3 being based on interviews with ten different patients, the situation may be clarified still further.

Studying Table VIII and its figures (and Diagram II), we are immediately struck by the fact that on most of the language and time measures P7 as compared with P8 shows a diametrically opposite reaction to D3.

It is essential to interpret the variations in the individual categories in concurrence with each other, in order to try and form a picture as to what actually happened in these two interviews and how the doctor's behaviour may have interacted with that of the patient's.

From Table VIII (patients) we see that P7 talked in total amount of time (AT) less and P8 more than their average amount of talking time based on all three interviews. Both patients' rhythm was quickened when talking to D3, i.e., their average duration of silent periods (AvS) as well as action periods (AvA) being shorter than when talking to D2 and D1, thus resulting in a shorter period of A + S (which we provisionally called tempo (4)—though it might probably be more correct to call it rhythm). However, the extent of reduction differs widely and characteristically from P7 to P8. P7 was reduced in his activity to a far greater extent than in his silence while P8 had much shorter periods of silence.

This state of affairs manifests itself most significantly in the amount of double silence (DS), that is the periods in which neither the patient nor the doctor said anything. There was in the interview P7–D3 more than twice as much mutual silence than the mean of the double silence period would make

TABLE VIII.—*Deviations from Means of Time and Language Measurements obtained from Interview Records of P7 and P8 with D3.*

(To make the figures comparable the original quantities were transformed into percentages over means.)

	P7.	P8.	D3–P7.	D3–P8.
AT	−16·4	+9·1	−21·7	−17·4
AvS	−11·0	−52·0	+21·0	−31·0
AvA	−62·0	−18·0	−94·0	−60·0
A+S	−55·0	−5·7	+3·0	−40·0
bs/ds	+6·0	+151·6	−9·5	+73·8
DS	+250·0	−160·0	+200·0	−143·0
FAP/FAD or FAD/FAP	+29·5	−28·9	−54·3	+74·8
KP/D or KD/P	−37·9	+23·1	+75·0	−67·0
WR	+30·3	−3·1	+6·1	−33·3
SR	−35·0	+15·5	−17·8	+28·5
N/S	+39·8	−4·4	+35·5	−38·5
V/A	−12·7	+7·8	−10·8	+11·6
Patients word output on subject of illness and mental state	−50·6	+29·1	..	..

AT = Total action* time in proportion to total duration of interview.
AvS = Average duration of silence periods.
AvA = Average duration of action periods.
A+S = Average duration interaction periods (action + subsequent silence).
DS = Total time of mutual silences in proportion to total duration of interview.
FAP/FAD or FAD/FAP = Relative frequency of action of patient and doctor.
K = Index of dominance (see page 189).
WR = Word rate (= number of words per minute of action).
SR = Percentage in total number of words of self-references.
N = ,, ,, ,, ,, of nouns.
N/S = Ratio of nouns over self-references.
V/A = Ratio of verbs over adjectives.

* The term action stands for speech and communicative gesture.

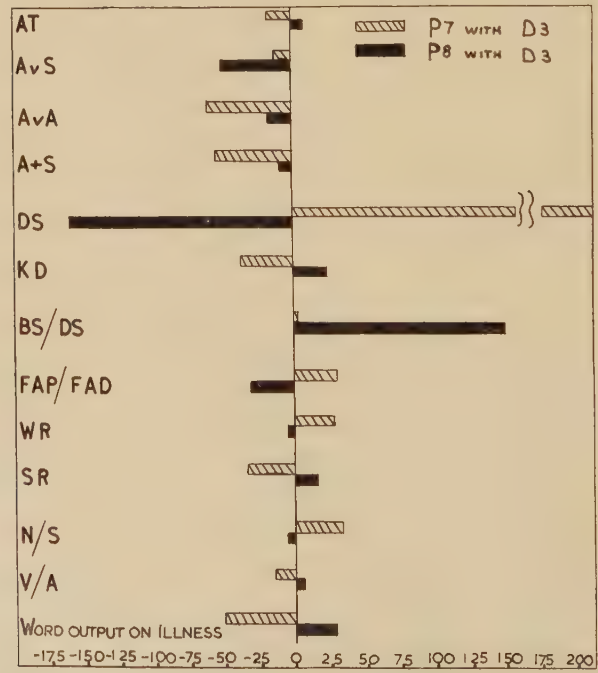

DIAGRAM II.—Deviations from mean expressed as percentages of mean P7 and P8 with D3.

one expect,* while in the interview P8–D3, DS was one and a half times less. Comparing the relative frequency of actions (and silence) of the patient in relation to the doctor, measured by a quotient whose numerator is the frequency of the patient's actions and whose denominator is the frequency of the doctor's actions (FAP/FAD) it can be seen that P7 started actions more frequently with D3 than with D1 or D2, and P8 started actions less frequently by about the same amount as P7. Summarizing the data so far, P7 in his interview with D3, talked less altogether, but talked more frequently than he did with either D1 or D2. Whereas P8 talked more altogether with D3 than with either of the other two doctors, but less frequently than might have been expected. At the same time P7 had periods in which he did not answer a question put by the doctor (double silence).

In trying to reconstruct this situation it may be visualized in this way: if a conversant starts speaking more often than his interlocutor but does not persist in it, it means that these periods are either of the conventionally brief kind, registering assent, and uttered intermittently during periods of speech activity on the part of the interlocutor (e.g., "yes," "I see," or nods), or they may be attempts to say something which fails to cut through the interlocutor's stream of talk. In both cases the relative number of periods of speech activity would be larger and their relative duration shorter than those of the interlocutor. In both cases too it would mean that the conversant was not dominant in interaction (that he was getting behind in the conversational round of exchanges), either freely assenting to this state of affairs, or else attempting to break through it, but without success. This situation is summarized in an index which we name K, and which is a product of two ratios: (*a*) of the total duration of the actions of speaker X to that of speaker Y, and (*b*) the ratio of the frequency of the actions of Y to the frequency of the actions of X. If, for want of a better term, we provisionally call this index a Dominance score,† it would, in the above form $\left(\frac{\mathrm{ATx}}{\mathrm{ATy}} \times \frac{\mathrm{FAy}}{\mathrm{FAx}}\right)$, be the measure of the dominance of speaker X. It yields the highest value in the case of the person who talks the longest and the least often (i.e., talks most of the time without stopping), and the lowest value in the case of the person who takes up the least amount of interviewing time but begins to talk or interjects most frequently. From Table VIII it is evident that in P7's interview with D3, K was considerably above and in P8's interview with D3 considerably below their respective average K indices. (In terms of the interpretation of this reading it would mean that P7 was far more submissive and P8 more dominant in speech behaviour with D3 than the behaviour of these patients in the interviews with D1 and D2 would lead one to expect).

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* In raw figures this means that while in the interview P7–D1, DS was − 3 per cent. (i.e., 3 per cent. of the total time of interviewing were simultaneous talk, as is signified by the negative DS score), and in the interview P7–D2, DS was 0 per cent., in the interview P7–D3 the period of mutual silence (S) took up 21 per cent. of the total time of the interview. In the case of P8, DS was 7 per cent. in his interview with D1, 11 per cent. of the total interviewing time with D2, and − 3 per cent. with D3, i.e., during 3 per cent of the interviewing time P8 and D3 talked together.

† Seven subjects of a previous experiment (6) had been ranked for dominance by three judges whose average agreement was ·76. Their mean rank order correlated with the index $\left(\frac{\mathrm{ATx}}{\mathrm{ATy}} \times \frac{\mathrm{FAy}}{\mathrm{FAx}}\right)$ ·94 (rank order r).

This situation is also reflected in terms of word output and word usage: P7 increased the speed of his word production considerably, P8 (slowed it down somewhat, P7 used far fewer self-references, P8 more self-references). The noun/self-reference quotient is higher for P7 with D3 than with D1 and D2, but lower for P8. The verb/adjective ratio is reduced for P7, increased for P8. The reduced verb/adjective ratio indicates, as a number of workers were able to show (1, 2, 3), the saturation of speech with action, emotion, and tension elements versus reflection or description and qualification. In other words the conversation of P7 contained relatively more words of description and qualification than of action and emotional tension, and that of P8 showed the opposite characteristics.

Our last datum is the proportion of words uttered on the various topics, particularly on the mental state, state of emotions and discussion of the patient's illness. P7 spoke far less with D3 about these subjects than his output with the other two doctors would suggest, while P8 spoke more about them with D3 than the other doctors. It is at this point that the doctor's influence makes itself more felt. For while the doctor cannot elicit more material on these topics than the patient is prepared to give, the *actual* amount of material produced in any particular interview on any particular subject must be conceived to be a function of the interaction between doctor and patient, i.e., to be partly dependent on the doctor's interviewing behaviour. This influence may derive from such obvious factors as the type of questions asked, and the kind of topics raised, but it may also rest on more intangible aspects of expressive behaviour in speech, some of which the various techniques and measures used in this investigation attempt to seize.

Having observed that P7 and P8 reacted linguistically in diametrically opposite ways to D3 (while they had not done so in their interviews with D1 and D2) the obvious question was whether D3 himself behaved differently with these two patients.

It is, of course, quite conceivable that two different individuals react in diametrically opposite ways to an interviewer whose interviewing behaviour remains unchanged from one case to the other. However, to satisfy oneself whether this was the case it was necessary to analyse D3's interviewing behaviour with these two patients. For in the event of their opposite reactions to him coinciding with a reversal in his own behaviour from one case to the other, we would have before us an example of interaction manifesting itself through the fluctuation of the various measures used in this investigation.

2. *D3 Interviewing P7 and P8.*

The analysis of D3's speech behaviour demonstrates clearly that such interaction did actually take place. Table VIII and Diagram III shows that D3's interviewing behaviour in his interview with P7, as embodied in the various time and language measurements, was the inverse from that in his interview with P8.

With P7, D3 had a relatively low activity rate, but with P8 a high one. His tempo of interaction (A + S) was faster than his mean for all ten interviews, when talking to P7, and slower in his interview with P8. His silences were longer with P7 and shorter with P8. His periods of speech activity were shorter than his mean in both cases, though somewhat longer with P7 than P8. During both interviews there was not much difference in the proportion of total time spent in talking to the two patients, but taking into account the difference in the rate of word production (236·4 with P7 and 148·5 with P8) the total word output of D3 for each minute of interviewing was 42·6 words

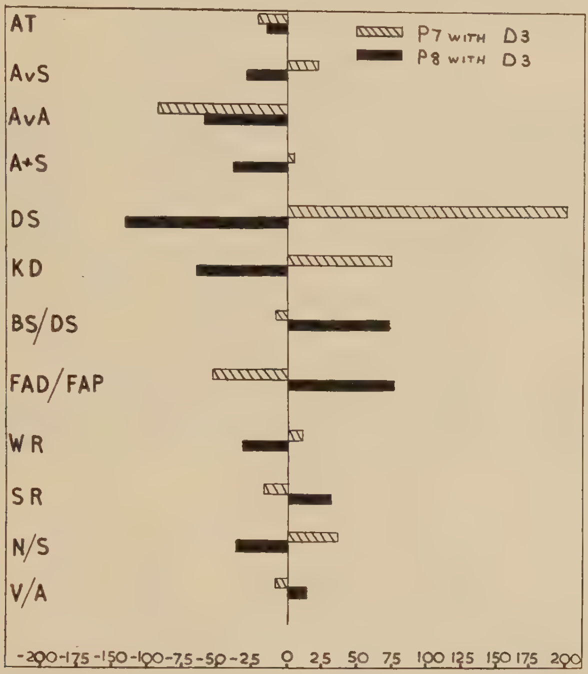

Diagram III.—Deviations from mean expressed as percentages of mean : D3 with P7 and P8.

with P7 and 28·2 words with P8. Altogether he presents with P7 a much more dominant picture—as perhaps one may call it—(K = 75·0) than with P8 (K = —67·0), and one in which adjustment is characterized by periods of mutual silence which were longer than this interviewer had with other patients. Contact with P8, on the other hand, is far more close and lively, with some overlapping talk rather than silence. With respect to parts of speech used, the language of D3 is distinguished by the fact that with P7 his language contains more than his mean proportion of nouns and less of self-references, the noun/self-reference quotient being well above the mean figure, the case with P8, on the other hand, being the reverse. His verb/adjective quotient in a similar manner swung into reverse direction, being below the mean when talking to P7, and above the mean, i.e., talking more in terms of action with P8.

All round we may say that with P7, D3 was more dominant, having a slower tempo of interaction (less participation, more indifference), a higher word output, a faster word rate, double silences and a quality of language indicating that he was more impersonal, his questions bearing reference to objective things rather than to the patient's self. The speech behaviour of P7 is characterized by unusually fast talking alternating with periods of mutual silence. The quality of the language of P7 and the content of his conversation shows a reduction, compared with the material he produced with the other two doctors, of topics of emotional import, or dynamic force (V/A), and of reference to the self.

VII. FURTHER ANALYSIS OF D'3S CONVERSATION WHEN INTERVIEWING P7 AND P8.

Origin of Discrepancy in Case P7.

The analysis of the records of P7 was pursued a step further in the hope of getting nearer to an understanding of the situational background of the intra- and inter-speaker displacement of the various linguistic modes of action and of content which we could measure. Working on the assumption that in the interviews the roles of the interlocutors were such as to invest the interviewer with the main initiative, D3's records with P7 and P8 were analysed in respect of type of questions asked and of responses offered in the two cases.

1. *Classification of Quantitative Data.*

Before discussing the qualitative aspects of D3's responses to the two patients in question, some figures which illustrate the quantitative side are given in Table IX.

TABLE IX.

	Tt.	SA.	FAm.	SVA.	FVAm.	FAm–FVAm.
P7	19·9	223	11·6	143	7·5	4·1
P8	10·6	208	19·6	67	6·3	13·3

Tt = Total time of interview in minutes.
SA = Sum of the doctor's actions during the whole interview.
FAm = Frequency of his actions per minute of interview.
SVA = Sum of doctor's verbal actions over the whole interview.
FVAm = Frequency of his verbal actions per minute.
FAm–FVAm = Difference between the frequencies of all actions per minute and verbal actions per minute giving a measure of the number of non-verbal actions per minute.

From Table IX it can be seen that the difference in the frequency with which D3 acted in each unit of time during the two interviews had an opposite trend when the verbal actions are separated from the gestural ones. The latter were mainly nods of the head. While D3 talked somewhat more often when interviewing P7, he nodded very much more often when interviewing P8. This we may take as an indication that his attitude towards the latter was more of a permissive or acquiescent kind than that towards P7.

2. *Classification of Qualitative Data.*

A classification was then made of all that D3 said under the following heads:

1. Questions initiating topics of conversation.
2. Questions following up topics initiated by the patient.
3. Arguments, remarks, observations.
4. Responses.

The following picture emerged: The overall distribution of the number of D3's verbal actions under these four heads differed considerably in the two interviews. These figures seem already an indication that D3 took a more active interest in what P8 had to say than in P7's remarks. For while only 20 per cent. of his conversation with P7 was devoted to questions *initiating* areas of discussion, as much as 30 per cent. of his conversation with P8 had that end in view. On the other hand, there were relatively more responses of the passive type in D3's conversation with P7 (68 per cent.) than in that with P8 (59 per cent.). The proportion of follow-up questions was the same in both interviews.

An even greater difference in D3's interviewing behaviour with these two patients emerges when we analyse the figures with respect to the kind of area touched by the questions and to the quality of response. While in the conversation with P8, 25 per cent. of all D3's verbal activity was given up to questions initiating the discussion of the former's *illness and mental state*, the corresponding percentage was as low as 3·5 in the interview with P7. The largest single group of questions with this patient (7 per cent.) occurred at the beginning of the interview, and were concerned with his name (an unusual French name). The patient's work, and his qualification for a job to which he aspired (but for which he lacked qualifications), accounted for a further 5·5 per cent., while 3·5 per cent. of the questions were concerned with testing the patient's information. Taking the questions initiating topics and the follow-up questions together, it is clear that D3's overt enquiries were concerned with the patient's occupational life far more than with his mental condition. With P8, D3 was bent mainly on obtaining material concerning the patient's mental suffering.* The nature of the material produced by the two patients showed, as was to be expected, the correspondence of the doctor's questioning with the material he obtained.

As to the responses, these were separately tabulated in Table XI, giving the following picture.

Three of the classes which emerged were identical for both interviews: (*a*) the class of "Yes," "Oh I see, yes," "Yes, I see," "Quite," "I see," etc. We shall call these the affirmative type of response; (*b*) The "Hms," and "Hum-hms," which we may call the reflective type; and (*c*) the repetitive affirmative type, such as "Quite, quite," and "Yes, yes."

Apart from these classes there was only one other major group of responses, which may be called interrogative responses, namely (*d*) the "Oh! really?"; "Did you?", "Have you?", "Are you?", "Indeed, indeed, indeed?". Items in this group occurred *only* in the interview with P7.

The most striking differences in D3's responses to P7 and P8 are to be found in the proportions of the type of responses employed. When interviewing P8, 33 per cent. of all his verbal actions were of the affirmative kind, as against 22 per cent. in the interview with P7, while the latter came in for a type of response (12 per cent.) which D3 never used with P8, namely the interrogative.

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* There was, to be sure, an objective basis for this difference of emphasis. P7 showed no signs of mental illness in his behaviour, but was rather more remarkable by reason of the absence of any symptoms. He had been in the hospital with anxious depression and was about to leave. Indeed, his problem at this stage was one of finding a suitable job.

TABLE X.—*Frequency Distribution of D3's Responses to P7 and P8.*

P7.		P8.	
Responses.	Frequency (%).	Responses.	Frequency (%).
Yes ! ; Oh I see, yes ! ; Yes, quite ! ; Quite, I see !	22	Yes, I see ! Yes, I see ! Hum, yes	33
Hum ! Hum ! Hum !	15	Hum !	15
Quite, Quite ! Yes, yes	12·5	Yes, yes	9
Oh ; really ; did you ; have you ; are you ; indeed, indeed	12		
No, no	3		
No	1·5		
That is good	1·5	No, yes	1·5
	67·5		58·5

We can thus see that the difference in the *quality* of the verbal activity of D3 when interviewing these two patients forms a meaningful background to the differences which were observed in his interviewing behaviour with them as described in *quantitative* terms, as well as with the differences in the quantitative picture of the *patients'* behaviour.

Continuing the search for a further explanation of this difference it was decided to track down the class of interrogative responses which had emerged as a specific feature in D3's language behaviour towards P7. The study of the context in which these appeared showed (*a*) that most of them were reactions to a certain exaggerated self-importance or gushing optimism in the patient's statements, e.g., when answering the question how he was getting on, " Oh, I feel better than I have been for years " (D3's response : " You do? ") and (*b*) that they were concentrated in the first 108 words of D3's output, i.e., the first 13·4 per cent. of his total output of 804 words. These 108 words were concerned with the subject of the patient's strange name and constituted as stated above the largest single group of the doctor's initiating questions. Nine of the total number of seventeen interrogative responses (i.e., 53 per cent.) occurred in this part of the interview, a figure which is far in excess of that expected in relation to its length. A chi-square calculated to test the significance of the deviation of the observed from the expected number of interrogative responses for this passage was 20·0, normally far beyond the 0·001 level of significance. We can therefore accept the results as significant in spite of the fact that the entry in one cell was below 5.

The indication is thus that D3's particular attitude in this interview with P7 as manifested in the various language and temporal aspects of his conversational behaviour emerged already at the very outset of the interview, when the subject of the patient's name was dwelt on at great length.

VIII. CONCLUSIONS.

The original purpose of this study had been to test a number of linguistic categories obtained from psychiatric interviews for consistency or relative invariance in respect of individuals. The conclusion arrived at was that some temporal as well as grammatical categories of speech behaviour are relatively constant, i.e., subject to habit formation of differing strength.

Two of the measures investigated in this study caught our attention by their capacity to combine general stability and plasticity : these were the speech rate (WR) and the self-reference percentage. There was, however, an essential difference between these two measures. The speech rates of doctors and patients ranged within the same universe (see Tables I and II), while the universes of self-reference percentages for the doctors and patients were widely separated. In other words speech rate was not only consistent for individuals but also independent of the rôle of the speaker in the interview, while the self-reference percentage showed invariance only within the doctor or patient groups, i.e., when the role and purpose of the speaker were held constant. In view of this superior degree of stability of the rate of speech, its discrepancies observed in individual patients, particularly P7 posed the question as to whether they were not indicative of reactions at a deeper level to changes in the situation-complex of the interview. The detailed analysis of all the measures available showed that the discrepancy of the speech rate was symptomatic of a total change in linguistic activity involved in the interviews concerned.

Shifts in any one category of linguistic behaviour seem to have been balanced by concomitant changes in some other categories. In addition, shifts within the conversational pattern of one speaker coincided with a rearrangement of the linguistic pattern of his interlocutor. Furthermore, the interviews which in the first place had been singled out on account of their discrepant speech rates showed wide differences of content, i.e., of the material elicited by the interviewer and the type of his questions and responses. Altogether a change in the subject discussed was accompanied by compensatory changes in the records of both speakers, of duration, rhythm, output and rate of talking as well as of some of the grammatical categories used. From this it seems that interaction operates by permeating the various categories of conversational behaviour, linguistic, temporal and in respect of content.

The picture which has thus emerged recalls Humphrey's (7) summary when surveying the field of evidence on the relation of thinking to the activity of language : namely that speech activity is a unitary process blending aspects of the utterance function of language with content or meaning into a closely-knit whole. Humphrey admits that the divsion of language into the three functions of utterance, reference and evocation, is useful for purposes of scientific abstractions, but rejects them as aspects of actual language behaviour. "The fundamental datum of speech is the fact that a man is *doing something*, namely talking *to* somebody *about something*. He is specifically reacting to a total situation complex comprising non-social and social—or, as Kantor (8) calls them, "bi-stimulational"—features." Our evidence is in keeping with this conception.

Our results have also shown that the constancy of linguistic units in the general structure of language, which linguistic science has established, is reinforced by personal habits of individuals. They also illustrate the *ad hoc* adaptiveness of this structure in accordance with the "total situation complex," maintaining balance internally as well as adjusting to the interlocutor.

VIII. SUMMARY.

1. Thirty interviews were recorded on an interaction chronograph for time measures, and in a speech recorder. They were conducted by three psychiatrists who each interviewed the same group of ten patients (composed of two sub-groups suffering from anxiety or depression respectively).

2. Certain time measures had previously been shown to be consistent for individual doctors and the two sub-groups of patients.

3. Owing to some spoilt recordings only 25 of the 30 interviews could be transposed to verbatim manuscript form.

4. A grammatical analysis and word count of the language used by doctors and patients was then undertaken. The following measures were subjected to analysis of variance: percentage of nouns and self-references in the total number of words, noun/self-reference ratio, verb/adjective ratio, word or speech rate measured by the number of words per minute of the conversation (i.e., of the individual's action time, *not* the interview time) or word rate.

5. The results were: highly significant consistency of word rate and self-reference percentage, and of noun/self-reference and verb/adjective ratios, and consistency at the 5 per cent. level of nouns and adjectives for the doctors.

6. For the patients only the verb/adjective ratio proved consistent at the 5 per cent. level, when the figures from all these interviews were compared, but word rate and self-references correlated highly only for interviews with D1 and D2, while in interviews with D3 discrepancies occurred.

7. The most extreme discrepancy occurred in the case of Patient 7 (P7) and as the discrepancy in the case of P8 was, on three counts, (word rate, self-reference percentages and action time), consistently in the opposite direction,. the two cases were subjected to a detailed comparative study, linking up the temporal and grammatical quantitative investigation with a structural topic analysis of the content.

8. Data from the available records suggest that word rate, self-references and action time for the patients varied concurrently, word rate correlating inversely with self-references and action time, and action time directly with self-references.

9. The juxtaposition of the discrepancies of P7, and P8 with D3, and of D3 with P7 and P8 over the range of 12 (for patients 13) measures of temporal and linguistic conversational behaviour (and patient's word output on the subject of his illness) shows that other modes of linguistic activity had also changed.

We were thus able to illustrate in terms of objective measurements that language functions as a unitary process blending aspects of utterance and of content into a closely-knit whole.

10. A classification of D3's questions and responses resulted in the location of that part of the interview where the discrepancy had its roots.

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THE EARLY HISTORY OF PSYCHO-ANALYSIS.*

By Ernest Jones, M.D., F.R.C.P.

It is rare for someone at my time of life to be in a position to make really original contributions to knowledge, though it does occasionally happen. More often we feel that we have something to offer that is generally called the "wisdom of experience," but it is a gift that a younger generation is apt to look at askance. There is, however, one field in which old age has an undisputed prerogative, and that is in being able to recall happenings in which younger people could have had no share. I propose to-day to confine myself to this modest claim and I shall be content if the illustrating of it arouses some interest in you.

Although the Royal Medico-Psychological Association has honoured me by electing me one of its few honorary members, an honour I very highly appreciate, I have to confess the startling fact that the present occasion is the nearest approach in my life to my attending any of its meetings, and this although I held at one time the position of a professorship of psychiatry. I mention this uninteresting, though curious, personal fact because it will serve as an introduction to what I have to say about past eras.

The reason for it has been that psychopathology of the neuroses, which has been my main interest, was then the domain of the neurologists, not of the psychiatrists, and it was from neurology that I moved on into it. Psychiatrists of the present day, with their intensive scientific training and wide range of knowledge can hardly form any picture of the low level at which their branch of medicine subsisted in my early days. There was, of course, no special training for budding psychiatrists, or alienists as they were then called, and no thought of any diploma to show that they had taken some interest in their subject ; and very few indeed took any interest. I remember a satirical friend of mine, himself an amateur psychologist, asking me once what alienists discussed at their meetings : "I suppose they read papers on an improved variety of Chubb lock."† When I was holding a resident appointment at University College Hospital, an Asylum Superintendent whom I had met telephoned saying he had a vacancy on his staff and could I think of anyone who would be willing to fill it. He added : "I don't expect him to be interested in insanity, but he must be able to play cricket with the patients." I understand that the terms of such appointments are considerably more onerous nowadays.

Nor did medical students fare any better in acquiring any knowledge of psychiatry. They were supposed to attend six lectures in the hospital and six demonstrations of cases in the asylum. Very few attended more than one of either and we took it in turns to sign up for friends at the others. If any students travelled as far as the asylum, playing games with the patients and cracking jokes with them was more to their taste than attending to the incomprehensible demonstrations. If they entered medical practice with some knowledge of the legal formalities needed to certify an insane person they had done all that they felt their duty demanded.

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* A paper read as a Maudsley Bequest Lecture, at the Royal Medico-Psychological Association, 31 July, 1953.

† The Notes and News section of the *Journal of Mental Science* of the time will supply factual information as to the subjects discussed at alienists' meetings.—*Editors.*

At this point I have, with your permission, to become a little autobiographical. I began my medical life as a neurologist, and although none of my contributions in that field would be remembered nowadays I am glad to think that some of the results have been silently incorporated into text books. My interest in the subject was early and extremely intense, so doubtless it had a neurotic origin. In the dissecting-room my teachers told me I was wasting my time acquiring an unnecessary detailed knowledge of brain anatomy, but I evidently felt that that part of the body was more likely than any other to yield the secrets that were perplexing me, about the nature of the soul, the purpose of life, and the means of controlling our animal nature. When a hospital student, I managed to work at Queen Square as a clinical assistant, and to continue in this position for some years even when holding resident appointments in my own hospital. I have vivid memories of the great men of those days who are but names to you: Charlton Bastian, Sir David Ferrier, Sir Victor Horsley, whose house surgeon I was, and many others. Sir William Gowers was a very great neurologist who was reported, no doubt apocryphally, to have maintained in an exalted mood that every day he had an infinite number of new ideas every one of which would make the reputation of an infinite number of neurologists. His real interest was in promulgating the use of Pitman's phonography among the medical profession and he published a periodical for this purpose which he mainly wrote himself. It happened that I had taught myself this shorthand at the age of twelve in a single week of intensive study—another profitable neurotic manifestation—and one day he observed me making notes in it. From that moment my fortune, so to speak, was made, and he showed me every kindness and help. Then there was the still greater Hughlings Jackson, to whom everyone looked up as the father of neurologists. He was one of the most modest men I have ever met. I remember his saying to me one day, with his hand on my shoulder: "If you want to understand epilepsy it would be best to forget everything that has been written about it and begin all over again." It was on a par with his famous prediction "If you want to find out about insanity you must first find out about dreams," one which has largely come true in our time. His name cannot be revered too much in the history of medicine.

In the meantime several of my friends were holding positions in various asylums around London, and I don't think all of them were good cricketers. One of them, Bernard Hart, who was then at Long Grove Asylum, has since made a distinguished name for himself as a psychiatrist, or perhaps I should say as a philosopher of psychiatry.* I used to spend many Sundays in the wards with those friends, familiarizing myself with the various manifestations of insanity in the hope of gleaning some understanding of what it was all about. The man who befriended me most was Dr. F. W. Mott, the real Father of the Maudsley Hospital. I used to accompany him regularly on his visits to Claybury Asylum where he had established the first laboratory in any London mental hospital. His interests, however, were centred in neuropathology and he had little clinical or psychological aptitude. Not that his attitude was a negative one in the latter respect ; he wrote me a letter in June 1910, when I was in Canada, congratulating me on "spreading the knowledge of Freud's valuable work." Nor must I forget W. H. B. Stoddart, a lasting friend of mine who was then resident at Bethlem.

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* The medical staff of Long Grove at the time included Hubert Bond, Henry Devine, Thomas Beaton and Edward Mapother! Their views on the "dangerous cattle" entrusted to their care are on record in numerous publications.—*Editors.*

When a few years later I attended a number of intensive courses at Kraepelin's Psychiatric Institute in Munich a new world opened up to me. There I found that mentally afflicted patients, instead of being regarded as dangerous cattle to be safely locked up and fed from time to time, were studied with absorbed interest from every point of view. Apart from the famous Kraepelin himself, for whom I did not, I may say, acquire any special respect, there was a large and elaborate staff who held daily meetings with demonstrations and discussions. Plaut was there conducting his serological researches into general paralysis, Alzheimer, a modest and delightful man, was then the greatest authority on histology of the brain, and there was a bevy of psychologists, both clinical and experimental. The year after I spent some months in Munich doing work on associations in the psychological laboratory, histological research under Alzheimer and of course attending the clinical demonstrations. All this gave me an entirely different idea of what psychiatry was, so when Sir William Osler suggested to me that I take charge of the Psychiatric Clinic the Ontario Government were proposing to open in Toronto I gladly accepted. There I made good friends with the leading personalities in the United States. Adolf Meyer, August Hoch, Morton Prince, James Putnam and others, but the psychiatric climate in Canada itself was at that time not much more propitious than in England, so after four years home-sickness took me back again to London where there were by then stirring signs of interest in psychopathology. In fact there was then a Psycho-Medical Society under the guidance of T. W. Mitchell and Douglas Bryan.

I have said that in those years psychopathology was thought to be the preserve of neurologists, not of psychiatrists. That was doubtless in deference to the popular belief that neurologists, being concerned with the nervous system, were the proper people to cure "nerves," as neurotic conditions were then called. I have often thought how embarrassing it must have been for such highly qualified experts in their own field to find they had to make a livelihood by treating for the most part entirely different affections of the nature of which they could have understood literally nothing. But somehow they managed to cope with that strange situation, which shows how adaptable human nature really is. The ignorance concerning psycho-neurotic conditions in the early years of this century was truly abysmal. The only people who thought they might have a mental aspect were a few hypnotists. Milne Bramwell in Yorkshire had made some excellent observations on the nature of hypnosis and in

London Lloyd Tuckey was practising suggestive therapy. But these were looked at very askance by the medical profession, and their activities were regarded as closely akin to quackery. For the science of neurology had decided that such conditions were disorders of the brain, not of the mind, and therefore it was the brain that had to be treated. A common explanation of them was that the speed of modern communication brought about by the building of railways imposed an excessive stress on cerebral functioning and exhausted the brain cells. These, therefore, had to be replenished by good feeding and the administration of phosphates, since it was known that the nervous system contained a higher proportion of phosphorus than any other part of the body. The Weir Mitchell treatment, devised twenty years before, fitted in admirably with this point of view. It could be carried out by anyone familiar with diseases of the brain. Sir Victor Horsley, for example, the celebrated brain surgeon, ran a nursing home in the Isle of Wight which he used to visit periodically to observe the progress, or otherwise, of his neurotic patients. As for hysteria, the drug *par excellence* was still valerian, dating from the days when its odour was believed to be obnoxious to the womb, which vied with the brain as the seat of the trouble. I found it very amusing when this magic property was dissipated by the administering of pure valerianic acid, the advantage of which was that it was odourless.

I will recall here two memories concerning hysteria. My friend Wilfred Trotter once remarked to me that hysterical convulsions were a great mystery I should try to unravel. He added : " One sees only the blood trickling under the door, but we know nothing of what tragedy is being enacted inside." What insight when contrasted with the teachings of my seniors! Three years later, when I had learned something about the extraordinarily complex nature of those tragedies, I was present at a lecture Dr. Mott delivered at the Maudsley Hospital. He demonstrated a very complicated case of conversion hysteria, doing nothing, however, beyond describing the physical symptoms. I fell into a reverie about the intricately beautiful construction that must lie behind that façade, and I imagined to myself that Mott was mistaking for a hovel what was really a magnificent palace. It was not for that reason, nor indeed for any other good one, that I did not enter that hospital again until last year when I delivered an address there.

I had been very familiar with the cases of multiple personality described in America by William James and Morton Prince and with the huge French literature on hysteria, the beautiful observations of Binet and Féré and the ingenious experiments of Pierre Janet. But in all the observational work that had been done I missed any concern with the dynamics of the processes in question, any explanation of what brought them about and what they all represented in the patient's mind. Trotter himself was inclined to regard psychoneuroses as disorders of social relations, of the " herd instinct " with which his name became associated. His idea was that certain people were so sensitive that they found various experiences and conflicts intolerable and directed their emotions into neurotic manifestations. I could find, however, no way of applying his herd instinct theory clinically. So I continued with investigating patients' memories under hypnosis in the hope of elucidating the intolerable nucleus, rather on the early Breuer-Freud lines. At that time I did not know of any other work being done in this direction. I remember being able to cure a case of complete amaurosis until we got to a point where the patient could see everything except his wife's face, a fact which was a distinct clue to the pathogenesis.

Then in 1905 Freud published his Dora analysis, the first of his post-neurological writings I came across. I hurriedly learned enough German to follow it and also read his *Studies in Hysteria*, which of course had not yet been translated. The *Interpretation of Dreams* I read only a year or two later. What impressed me most to begin with was that there was a man who actually listened to his patients, a thing I had never heard of before. It was evident that every single utterance of their's was taken into account just as if it was a physical sign in clinical medicine. Then there was the matter of symbolism, and his freedom in admitting the significance of sexuality, both of which I had been prepared for by my reading in anthropology and comparative religion. Above all there was Freud's constant search for meaning, purpose, motivation, just what I had been wanting. So I became a willing adherent of the new doctrines.

In that year, 1905, forty-eight years ago, I ventured on the practice of psycho-analysis. I well remember my first case, the first one to be analysed outside of German-speaking countries. She was the wife of a well-known New York neurologist, but I may add it was not he who sent her to me. As a result of the analysis she procured a divorce, and her husband pursued me with considerable venom after I had moved to America a couple of years later. He was sure to turn up whenever I read a paper at a meeting or congress and counter it with abusive remarks about the evils of psycho-analysis. It was my first experience, and certainly not the last, of finding that adverse criticism of psycho-analysis was not always as objective as it pretended to be.

In 1907 I made Jung's acquaintance at the International Congress of Neurology in Amsterdam and later that year visited him in Zurich. We there discussed the feasibility of holding a special congress to discuss Freud's work, and he arranged one for the following April in Salzburg. I have given a full account of the first psycho-analytical congress elsewhere, so will not repeat it here. Brill of New York and myself were the only non German-speaking analysts to attend it. There was one other British visitor besides myself, Wilfred Trotter. It was the occasion when I first met Freud himself, an event I had greatly looked forward to. As an example of Freud's wide range of interest I may quote his first remark to me when I was introduced to him. He said : "From the shape of your skull you can't be an Englishman ; you must be a Welshman." Whether he divined this from my cranium, which I very much doubt, or from my name and perhaps facial expression, what struck me about the remark was that it was the only occasion I ever found anyone in Austria or Germany who knew of the existence of my native country. Freud was then fifty-one years old. His build and complexion were those of someone who lived a sedentary life. He had quick, restless, almost nervous movements. His expression was slightly anxious but mobile and very observant. His dark brown eyes were perhaps the most prominent feature, quickly darting here and there with a very penetrating glance. His paper was the first on the agenda, and he delivered it without any notes. It was a description of a case of obsessional neurosis, which he published later, one that has been called that of " the man with the rats." He spoke for three hours and so interestingly that we were all surprised to find what time had flown. Then he paused, saying : " I am sure you have heard enough." We protested, so he resumed the account of the case and went on for another hour. That he could hold an audience in this fashion was both because of the novelty of what he had to say and also his extraordinary gift for orderly presentation.

After the Congress I spent a few days in Vienna with him and then moved on to Budapest to see Ferenczi, his leading adherent. Except during the war I visited Vienna once or twice a year, sometimes spending a couple of months there. In spite of an undefinable inner reserve Freud was very easy of approach, and he was a great talker—often till two or three in the morning. This sometimes embarrassed me, since I knew that his first patient was at eight in the morning and that he had a hard day's work in front of him. He was also a good correspondent, and I possess some six hundred letters he wrote to me with, incidentally, five thousand he wrote to other friends or relatives.

Perhaps you would now like to hear a little about some of Freud's early supporters. He had worked quite alone for several years, but about 1902 a small number of those who attended his University lectures began to take a serious interest in his ideas and they used to meet at his house once a week to discuss their experiences in attempting to put his methods of treatment into practice. Most of them did not pursue the study very far after their initial interest was exhausted, but by the time I first attended these meetings in 1908, there were several who have since made a name for themselves. Among the oldest members were Adler, Federn, Hitschmann and Stekel.

Sadger, who joined in 1906, used to take shorthand notes of the sessions with his patients, a practice Freud frowned upon. He was an uncouth person. Once when he was placed next to a strange woman analyst at a banquet he fidgeted for a while and then began the conversation with the question : " Do you busy yourself with masturbation?" a phrase which in German is still more ambiguous. Stekel was a more interesting person ; he was a thoroughly good fellow at heart and a very agreeable companion. He had no scientific conscience so no one placed much credence in the experiences he reported. It was his custom to open a discussion on whatever the topic of the day might be with the remark : " Only this morning I saw a case of this kind," so that Stekel's " Wednesday patient " became proverbial. He was a fluent writer and would have made a successful journalist ; in fact he earned his living for some years in that way. More important, however, was the fact that he was a very gifted psychologist, with a remarkable flair for detecting the hidden meaning of the patient's communications. Unfortunately this was combined with very deficient critical judgment, so that after a few years his uncontrolled speculations brought about a complete separation from other psycho-analysts. The next to join the group was Adler, who later achieved a reputation by providing a much simpler theory of the mind than Freud's, one that many people eagerly accepted with relief as a pleasanter alternative. He was a surly and even sulky person, always with a grievance, but when I met him many years later I was pleased to observe that success had given him a much more benign appearance. Freud had, rather unwisely, tried to appease him by making him President of the Vienna Society in his place, but this did not serve for long. He was by nature a social reformer, or perhaps educator, and he was quite deficient in any psychological insight. He never even glimpsed what went on in the unconscious part of the mind, which no one could have said of Stekel.

The next member to join was Hitschmann, who still practises analysis in Boston. So he and I have been practising analysts longer than anyone else, even fourteen years longer than Freud was. His writings on the obsessional neurosis are still perhaps the best we have. About the same time came Federn, who died a painful death in New York last year. His contributions to the psychology of ego functioning are outstanding. A year later Otto Rank joined the group and became for many years its extremely efficient secretary. He was a very capable person administratively, and his labours in the early days of the publishing firm Freud founded in Vienna were simply stupendous. He did everything, bought the printer's type and the paper, saw everything through the press and then tied up the parcels and took them to post himself. He had an uncanny flair for the interpretation of literary, legendary and mythological material ; he said to me once he found it so easy that it almost bored him. He was the first lay analyst, and with his entry into clinical work began to find difficulties in applying his knowledge of the unconscious which had seemed so easy to him in other fields. Intellectual appreciation is a very different matter from affective appreciation. Rank was devoted to Freud and was of great personal assistance to him, especially during the hard years of the first World War. Not long after it was ended, however, he tried to simplify psycho-analytical theory by making everything centre on one factor, and one not easy to investigate objectively, his well-known idea of the birth trauma.

At this point I will leave my more personal memories and say something about the early beginnings of psycho-analysis. What I have to say is based on researches I have been carrying out in the last few years on the data of Freud's early life and the genesis of his ideas, and they will, I think, be new to most of you. Freud has been regarded as a revolutionary genius who introduced novel and disturbing ideas. The first half of this sentence is doubtless true, but the second half needs qualification. As a result of my researches I came to the unexpected conclusion that hardly any of Freud's early ideas were completely new. Perhaps the two for which novelty can best be claimed—both, it is true, of great importance—were his theory of the dissociation of affects from ideas and his explanations of dream life. We shall see, however, that this conclusion in no way detracts from his originality, since this had another provenance.

Let us consider the ideas that are generally thought to be most characteristic of him, especially in his early period. They are his division of mental processes into two classes, which he termed primary and secondary respectively ; his insistence on the reality and importance of unconscious mental processes and on the conflict between them and conscious ones ; the significance of sexuality first in the aetiology of the neuroses and then in life in general ; the existence of infantile sexuality ; the nature of unconscious symbolism ; the phenomena of repression and resistance ; the employment of free association as a therapeutic method ; the significance of childhood experiences for later life ; the rigid determinism of mental life ; the constancy principle which asserts the tendency to revert to a previous state ; the activity of two censorship barriers in the mind ; the concept of summation of excitations ; the idea of somatic compliancy as in hysterical conversion ; and the fundamental importance of the pleasure principle in mental life. This is a formidable list of ideas, which I cannot discuss here in detail, and yet it can be shown that there are broad hints of all of them in the writings of previous workers with which Freud was thoroughly familiar.

It is a curious fact that the idea of an unconscious mind was much more familiar and widely accepted in the nineteenth century than in the twentieth. Poets had of course long observed that their inspiration often proceeded from some inner source unknown to them, and many philosophers, Schopenhauer being prominent among them, had on theoretical grounds often postulated its existence. So did respectable people in our own profession, such as Sir Samuel Wilks, whom I remember as President of the Royal College of Physicians fifty-five years ago. The arguments in favour of its existence had been perhaps most fully marshalled in von Hartmann's well-known *Philosophy of the Unconscious* in the eighteen-sixties. In the early part of the twentieth century, however, a fierce opposition arose against the very idea, and both philosophers and psychologists joined in asserting that anything that was not conscious must be physical, as Carpenter had maintained in his phrase " unconscious cerebration." That may very well be true, but if so it must be equally true of conscious processes as well, for the fact remains that both are describable only in the same language and cannot be distinguished except in the one respect of consciousness being present or absent. Among the many outbursts I recall in this empty controversy there was one particularly fierce one by the psychiatrist Dr. Charles Mercier, an able man and a pungent satirist. With scathing ridicule he likened the idea of an unconscious mind to a navigator appealing to an imaginary " outboard " attached to his ship and ascribing to it all the faults in navigation or strange happenings he was unable to account for.

How much of the change from the one century to the next was connected with Freud's having for the first time revealed the actual *content* of the unconscious it is hard to say, but it certainly did not improve matters, and it was much more comfortable to continue in the belief that only noble inspirations arose from unconscious cerebration, the rest being the product of Freud's evil mind.

Similarly with the division of the mind into two great classes. That had often been proclaimed on theological and philosophical grounds. Man's higher nature and his lower animal nature were familiar conceptions, and Meynert, Freud's chief in the Psychiatric Institute in Vienna, had attempted to express the division in anatomical terms. According to him the moral part of man was served by the cerebral cortex and his immoral part by the basal ganglia.

It was indeed Freud's friend Breuer who clearly effected the distinction between what he called the free-flowing energy of the primary mental processes and the bound or inhibited energy of the secondary ones, an idea which Freud maintained represented the deepest piece of insight in psychology.

What is called the Herbartian psychology was dominant in Vienna at the time of Freud's youth, and his teachers, particularly Exner and Meynert, were fully imbued with it. Herbart, seventy years previously, had clearly enunciated the idea of unconscious mental processes and also their incompatibility and conflict with conscious ones. He actually used the word "*verdrängt*" (repressed) to describe their being extruded from consciousness. He postulated further two thresholds in the mind and these correspond very closely with the two censorships Freud held exist between the unconscious and preconscious and between the preconscious and consciousness respectively. As for psychological determinism, to which Freud adhered so firmly all his life, Herbart had written "Regular order in the human mind is wholly similar to that in the starry sky." Herbart also held that the body responds to affects to a varying extent in different people, and described this by the term "physiological resonance," one which must remind one of Freud's "somatic compliancy" in conversion hysteria.

Since all these ideas were in the air it does not seem very important to ask from which teacher Freud acquired them. Some have insisted on his debt to Meynert, others to Breuer, and so on. But in the course of our researches a very interesting fact has come to light. Dr. Bernfeld, whose recent death we greatly deplore, found that Freud's school in Vienna had preserved all the records of that distant period, and he was able to resuscitate a complete list of his fellow-pupils, of Freud's position in class in every year, his examination marks in the various subjects, and even the text-books prescribed for his reading. Now in his last year at school one of these was a book on psychology by a man called Lindner, who maintained that no other ideas in psychology were worth considering besides those of the great Herbart, and he described them in full. So Freud must have been imbued with them from his very boyhood.

Fechner, whom Freud greatly admired, continued in the same tradition. Freud in his writings ascribes to him the constancy principle which plays a central part in his own doctrines. It was evidently connected with the Mayer-Helmholtz doctrine of the conservation of energy. The idea of "threshold" plays a central part in all Fechner's writings and it was he also who likened the mind to an iceberg whose course is determined not only by the winds that affect the surface but by the currents in the depths that move the submerged nine-tenths. Fechner, whose name is familiar to you all in the Weber-Fechner logarithmic law of sensations, made a gallant attempt to fulfil Herbart's dream of a mathematical psychology, one in which the elements were to be stated in terms of measurable quantities. This was also a dream of Freud's for some time, but unfortunately—or perhaps fortunately—he was no good at mathematics. A relic of it is his conception of affects as definite quantities which in time would prove measurable.

Meynert, the teacher he thought most highly of, followed on the same lines. It was perhaps from him that Freud got the idea of summation of excitations, a concept Meynert often used. It was almost certainly from the observation of Meynert's amentia, nowadays called acute hallucinatory psychosis, that Freud first got the idea of wish-fulfilment in psychopathological processes. Griesinger, another psychiatrist, was imbued with all the ideas we have just mentioned. In his opinion the unconscious was mainly affected by impressions emanating from the internal organs and consciousness by those from the outer world. This was exactly Freud's own view.

That the sexual instinct is a prime motor in human life is an opinion that had been voiced by many thinkers, from Plato to Schopenhauer. And that it is a dominant factor in the causation of neurosis was a sentiment that had been felt rather than expressed throughout the ages. Hence the constant, though mistaken, advice to hysterics to get married. The very name hysteria, from the Greek for womb, betokens the same belief, although in the nineteenth century the last stage in prudery had displaced the lesion from there to the cortex. Freud himself related three occasions when he had been given broad hints of the sexual aetiology of hysteria, by Breuer, Chrobak and Charcot respectively. How thoroughly he had forgotton them is shown by his remarking in the late nineties on how surprised he had been to discover that aetiology in his patients and that none of his teachers had held such a view. It is very doubtful, however, whether these forgotton remarks played much part in the conclusions he had come to; they were based far more on his own clinical experience.

Nor was Freud the first to call attention to infantile sexuality. Apart from the fact that he once ruefully quoted to me, that every nursery maid knows about it, a children's specialist in Budapest, Lindner, had in the seventies of the last century pointed out that sucking at the breast has a double function in infancy, a nutritive and an erotic one.

The technique of free association for therapeutic purposes Freud evolved by slow degrees in the course of unravelling his patients' anamneses. But before then several writers had pointed out its value in the obtaining of ideas for literary purposes. One of these was Freud's favourite author in his adolescence, Ludwig Börne by name, and he had surely read the passage in question. Moreover, Dr. Zilboorg, whose erudition in medical psychology is unbounded, has recently called attention to an exposition of free association by no less a person than Sir Francis Galton in a number of *Brain* which Freud certainly possessed and read.

So we see that most of the elements that went to make up his later theory of the mind had been lying about in scattered places, ready for him to pick up and make use of. We also see here the difference between mere cleverness and the true originality of genius. What to the others had been little more than bright ideas were to Freud important conclusions to be taken with the utmost seriousness, to be carefully explored and tested and then woven into a comprehensive theory.

Perhaps the best illustration of this difference is the example of childhood life. When Wordsworth wrote that the child is father to the man he was simply voicing a piece of proverbial knowledge which everyone knew to be true. But no one knew *how* true it is before Freud traced in minute detail the connections between the earliest and often unconscious impulses of the infant and the later structure of the adult character. Think, for instance, how astonishing it would have seemed to Wordsworth to be told that whether someone was an optimist or a pessimist depended on how he had responded to his erotic enjoyment of sucking as an infant.

As is well known, Freud worked alone for several years. He suffered greatly from loneliness in those years, although the loneliness was more subjective than objective. Besides his wife and six children, to whom he was exceptionally devoted, he led a pretty full social life and had many excellent friends. The intellectual loneliness, which is what he specially minded, was partly relieved by occasional meetings with his great friend Fliess of Berlin and a regular correspondence with him. This has fortunately been preserved and published together with several manuscripts Freud sent him from time to time. They constitute an invaluable source for studying the early phases of Freud's ideas, the errors he at times fell into, and the modifications he gradually introduced. They have thrown a great light on the way in which those ideas were evolved.

His loneliness in the scientific circles of Vienna was, however, far from being a passive one. It could better be termed an active ostracism. Little reference was made to him in public, but Freud could hardly escape hearing in devious ways something of the things said of him in private. He was a crazy crank, a paranoiac with a diseased imagination that invented fantastic mental connections, and in any case he must have a very foul and unpleasant mind to talk and write about intimate topics with the freedom he did ; he showed none of the reserve and delicacy that properly kept such topics in the background. It could not have been agreeable to know that this was how his former colleagues from his old hospital thought of him, but Freud was big enough not to be crushed by it and to accept his inevitable fate. He went straight on with his researches, investigating one new field after another. He had the genuine humility of a great man and was not uplifted by any illusions about his work. He was confident that he was making some contribution to knowledge, though how important only posterity could judge. More valuable to him than this altruistic thought was the personal interest he derived from finding out new things, wresting for himself some of Nature's secrets. This delight in discovery for its own sake was perhaps his greatest pleasure in life.

Early in the century he was joined by half a dozen adherents in Vienna. They were unimportant general practitioners, unknown in the scientific or professional world, and they were all Jewish. It was a small and modest beginning of a following, but better than nothing, and Freud made the most of it by instituting weekly discussions. In these circumstances how much he must have welcomed any sign of recognition from the world outside. There had been in England a few sympathetic reviews of his writings, by Mitchell Clarke, F. W. H. Myers and Havelock Ellis, but nothing at all in any other country. Before the first decade was over, however, two events in the outer world gave him great pleasure. The first was the news that the Professor of Psychiatry in Zurich and his assistant, Bleuler and Jung respectively, were not only taking his work with extreme seriousness, but had carried out controlled researches in experimental psychology that fully confirmed it. Moreover, they were extending his conclusions to a new field, that of insanity. In the spring of 1907 Jung came to Vienna to visit Freud, an exciting event for both of them. They had much to talk over together. In the following spring the first Psycho-Analytical Congress was held at Salzburg. It was a small affair, but, as some of you may have seen this week, such congresses have nowadays an attendance of many hundreds of analysts. The second event took place the year after. It was an invitation from Stanley Hall, the President of Clark College in Massachusetts, to deliver a course of lectures at the anniversary celebrations they were holding. I was present on that occasion also, and I well remember the poignant tone in which Freud thanked the President for what he called " the first official recognition of our endeavours."

It was by then becoming evident that Freud's work could no longer be simply cold-shouldered. The ignoring was replaced by a spate of so-called criticism, which in most cases extended beyond an expression of mere disbelief into the sphere of abuse. In Germany, in particular, this was expressed in the coarsest terms. Knowledge of Freud's work had at that time not extended far beyond the German language. An eminent professor of psychiatry expressed the view that a *cordon sanitaire* should be placed around this " psychical epidemic among doctors," and another one, at a congress in Hamburg shouted, with an appropriate bang of his fist on the table, that this was no occasion for serious criticism : " it is a matter for the police." In private talk there was, of course, even less restraint, and no occasion was missed for ribald jokes at Freud's expense. I was working at the Psychiatric Clinic in Munich just after Freud's paper on anal erotism appeared, and it was thought very funny to ask when it would become compulsory for everyone to have their erotogenic zones painted red so as to indicate their character.

Freud took all this quietly, although it naturally did not increase his respect for the objectivity of his German colleagues. He said to me once : " They may disbelieve my theories, but I am sure they dream of them."

Every country to which psycho-analysis has been new has one after the other been swept by storms of criticism and abuse, but they nowhere descended to the pitch of vulgarity that they did in Germany. Such storms die down in time, although one can never forget the unpleasantness of living through them, and they are then replaced by some degree of toleration, if not understanding. The history of startling novelties in science presents a characteristic curve, the first phase where they are derided as both erroneous and impious, a phase of tolerance, and then one where they appear to be quietly accepted as obvious or even old-fashioned. In that last stage, however, the apparent acceptance does not necessarily imply a real understanding. Einstein's theories, for example, are accepted by thousands of people who certainly cannot understand them. All that is a matter for the social psychologist. What the medical psychologist can contribute to our knowledge of the phenomenon is the discovery, in itself very difficult to appreciate properly, that there are many degrees in the process of belief or acceptance of an idea by the mind. Indeed, we commonly speak of doing lip service to a belief when we do not take it very seriously, a common enough occurrence in the field of religion. We now know that belief is far more of an affective process than a purely ideational one. In the stage of respectability that psycho-analysis has reached in England and America there is an increasing danger of the insight we have by such hard work gained into the nature of the unconscious mind becoming more superficial. I will conclude what I have had to say with a true story from analytic practice. On an occasion when a particularly striking piece of confirmatory evidence had emerged the patient exclaimed: "I knew that Freud's conclusion on this point was true, but I never knew until now *how* true."

FURTHER STUDIES ON ENDOCRINE TREATMENT IN ADOLESCENCE AND EARLY ADULT LIFE.*

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Although endocrines have often been used in the treatment of various psychiatric states, the measure of success has been small. Oestrogens have improved certain forms of involutional depression, and thyroid has been successful in the treatment of cretins, depression secondary to myxoedema, and in periodic catatonia. The following reports on the use of dehydro-isoandrosterone (diandrone) and oestrogens suggest a useful development in endocrine methods, either singly, or in certain cases, in combination.

I. Diandrone.

One of the 17-ketosteroid excretion groups is the beta group comprising 8 to 15 per cent. of the total output in the urine of both men and women. Callow *et al.* (1938, 1939) regard the beta fraction as the equivalent of diandrone, and as arising solely from substances produced by the adrenal cortex. It follows that beta ketosteroid excretion should be an index of at least one aspect of adrenocortical activity. Interest in the use of diandrone was stimulated by the studies of Reiss, Hemphill *et al.* (1949) on schizophrenic patients. In association with Strauss (1952) our first trials with this drug were conducted in a small group of adults of schizophrenic and schizoid psychopathic type. The illnesses were relatively mild even if chronic, or only slowly deteriorating. Treatment was limited to those of abnormal 17-ketosteroid excretion, in particular low beta excretion. Some showed a favourable response, but no definite correlation between type of response and beta fraction was demonstrated.

Since the striking developments of personality during adolescence are normally paralleled by considerable increases in adrenal and gonadal activity, it seemed that diandrone should be tried in juveniles or adolescents who were fundamentally immature and lacking the normal personality development characteristic of this critical period of life. The steroid was therefore tried in a group of such inadequate types. Some of these inadequates also showed schizoid trends, but others had neurotic or depressive clinical pictures. Many showed evidence of physical immaturity. This group were selected entirely on clinical grounds, since fractional steroid excretion analysis has not been possible until recently. None the less, in a small pilot study by Sands and Chamberlain (1952) results were more decisive than in the adult group.

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* Based on a paper read at the Quarterly Meeting of the Royal Medico-Psychological Association at the Central Hospital, Warwick, May, 1953.

The case material of this present paper comprises some 57 patients, of whom 38 were male juveniles or adolescents between 12 and 20 years, 6 females between 11 and 37 years, and 13 adult men between 21 and 37 years. The great majority were selected on account of various forms of constitutional inadequacy. A small group were selected for control reasons, and were psychopathically aggressive and schizophrenic. The following cases illustrate a favourable response to the drug.

Case A.—A boy, aged 14, was referred to his local child guidance clinic on account of truanting, since he had found the other boys at school too rough. He was subsequently sent to St. Ebba's as a suspected case of schizophrenia. For many years he had shrunk from personal contacts, been sensitive, shy and latterly more solitary. Recently he had become morbidly preoccupied with thoughts on abstruse topics beyond his years, chiefly psychology and religion. This was confirmed on admission when he appeared vague, emotionally flattened and disjointed in thinking. In the ward he read a lot, wrote many letters, helped with domestic jobs, showed interest in philosophy, but mixed little with others. After a month's control period with routine investigations and treatment of patient and his family, yet with little change, he started diandrone therapy 1 c.c. (20 mgm.) on alternate days. After 10 days he improved, being more active, more in touch and practical in his outlook. Eventually his religious and other preoccupations disappeared. The drug was stopped and he was discharged, much improved. Six months later he was reported to have a job at a printers, but still apt to speculate on religion, and to be readily teased by other youngsters.

Case B.—A youth aged 15½, was referred after a suicidal attempt with aspirin and by suffocation with pillows. By disposition he had been a rather solitary type, prone to worry and be preoccupied over the future. In the last six months he had become disinterested, moody and depressed. His mother showed similar personality trends, and both had been upset by a difficult neighbour. After admission he was depressed and displayed various psychosomatic symptoms, and it was noted that he was undersized for his age, with under-developed genitalia and pubic hair. Though improved by psychotherapy and modified insulin, he continued to show marked feelings of inferiority, guilt over masturbation and a sense of failure. On diandrone, mgm. 10 daily, he regained much confidence, was able to discuss his case more dispassionately and to co-operate more adequately in psychotherapy. Eventually he became rather over-stimulated and even tended to bully other boys. Far from feeling a failure he expressed his willingness to try a job. A year later he was seen while at work as an office junior, having been 10 months with the firm, also doing night school and living a full social life.

Indications for the Use of Diandrone.

(*a*) Young inadequate psychopathic types of personality characterized by timidity, lack of social confidence, feelings of inferiority, apathy, vagueness, mixing uneasily with others, and at times effeminate or homosexual, responded well, even if some were complicated by schizoid, hysterical or anxious traits.

(*b*) Although diandrone is not a treatment for schizophrenia in any general way, and indeed may make some such sufferers worse, it has a use at a certain stage of, and in some forms of, this disorder in conjunction with other methods, as shown later.

(*c*) Stammering, when arising on an inadequate and anxious basis, has been successfully helped by diandrone. Verbal confirmation of this has lately been given me by Dr. W. A. Stevenson.

(*d*) A further direction in which the drug has been useful is in improving rapport and accessibility to psychotherapy.

Another case showed little response to six sessions of psychotherapy until diandrone was also given. Equally caution is needed, since if the patient is unable to handle the material raised by psychotherapy, diandrone may make him worse and precipitate depression. As one patient said, "You are putting high-octane fuel into an old car," or more appropriately, "new wine into an old bottle."

Finally, all the patients who improved with diandrone were less than 23 years of age. The response to diandrone was usually evident in from one to three weeks, according to dose and sensitivity. The first sign was generally an increase in activity shown by improved performance at school or occupation, and by ability to discuss feelings and future aims. Confidence improved, and relations with others became more normal. While a mere proneness or tendency to homosexuality appeared to give way to more definitely heterosexual interests, there was no evidence that any conversion from an *established* homosexual attitude to one of heterosexuality could occur. In fact those definitely homosexual became more so under diandrone, leading to discontinuance of the drug. Mood, *per se*, was not directly influenced, but arising out of improvement there was often disappearance of depression. Weight was either gained or maintained, but without other physical maturation or change.

Contraindications are :

I. A history of aggression in the personality before breakdown, e.g., chronically aggressive psychopathic types, in whom diandrone can provoke attacks of rage, even with comparatively small doses.

II. In mania and in aggressive schizophrenics without history of earlier inadequacy. Even in inadequate schizophrenics, some caution is required.

III. Chronic homosexuality or other established sexual abnormality, which may be flared up to acute phase.

Dosage.

Usually ranges from 5 to 30 mgm. in tablets by mouth. There does not seem to be any special advantage with injection methods. Individual responses vary greatly, and up to 100 mgm. has been given to a middle-aged man without apparent effect. The drug may have to be continued for several months. Little information is available yet on long-term treatment, but while some patients continue well after the drug has been withdrawn, others relapsed in varying degrees. More work is required to determine the categories in which relapse may or may not be expected, and how dosage should be managed. Diandrone is not absorbed from under the tongue, but mainly from small and large bowel.

Discussion and Mode of Action.

Diandrone will inevitably be compared in androgenic activity with testosterone. Their differences are that while testosterone promotes increase in weight, testicular development, potency, and secondary sex characteristics, diandrone exerts an androgenic effect in a social and psychological rather than a physically sexual field, promoting a masculine activity aggression, self-confidence, small or no increase in weight, and little noticeable effect on secondary sex characters in men, such as growth of hair. In the female cases, one was thought to have shown increase in axillary hair.

A most important point is that the drug has proved very consistent in its action on those features of personality which lie between extreme inadequacy on the one hand and extreme aggression on the other. There is little evidence that it directly affects anything else. It brings the inadequates near normal, it makes aggression flagrantly worse, whether the aggression be expressed through psychopathic, manic or schizophrenic channels. Dosage can be regulated by careful watch for undue irritability and overactivity appearing in the formerly timid, shrinking violet. The results of this transformation on the patient's associates are often quite entertaining! One is reminded of the hen run, the pecking order may be reversed.

Previous studies, such as Cleghorn's 25 Addisonian patients (1951), have been concerned with cases where the *total* adrenal function was disordered, its extent reflected in total 17-ketosteroid excretion, and related to a demonstrable adrenal pathology with cortical atrophy. In cases suitable for diandrone treatment, some have a low beta ketosteroid output but no consistent alteration in total 17-ketosteroid excretion has been found yet, nor any pathology described.

The nature of the action of diandrone shows similarities with the better known adrenal steroid, cortisone. Although in cortisone's chief indication, rheumatoid arthritis, there is some evidence to suggest reduced adrenal function, no disorder of total 17-ketosteroids is usually apparent, nor is the adrenal the subject of any known pathological change in this disease. The therapeutic value of cortisone in rheumatism, asthma, etc., would appear to lie in its power to alter the hypersensitivity of certain connective tissues. Clinically an alteration of sensitivity of the nervous system to emotional stress by diandrone would be in accord with the response in inadequate and aggressive psychopathic personalities. In considering the way in which diandrone conforms to any general concept of hormonal function, it should be noted (*a*) that it does so in as much as, like other hormones, its action is essentially to facilitate a process, and (*b*) it serves one of the organism's fundamental needs. We are all familiar with the activities of hormones in relation to the promotion of certain physical changes. The outstanding point about diandrone is that perhaps for the first time we have a hormone promoting a specific type of mental change or development. The adrenal is already much identified with hormones promoting physical resistance to stress, and from these mainly clinical studies the indications are that in the young diandrone is perhaps one factor in the development of mental resistance to stress.

II. Oestrogen Treatment in Selected Psychiatric Disorders.

A Philadelphian physician, Dr. C. W. Dunn (1940), and Drs. F. L. Golla and R. S. Hodge (1949) of the Burden Institute, Bristol, appear to have been among the first to employ oestrogenic substances as a form of chemical castration to reduce excessive libido in the treatment of sexual offenders. Indeed Dr. Golla claimed the use of oestrogens to be more efficient, since not only was it unnecessary to inflict a mutilating operation, but the reduction in libido was more complete. He pointed out that it was erroneous to assume that castration resulted in the complete disappearance of libido, since various writers (1924, 1928, 1933, 1943) had shown this to be untrue. The partial effect of castration may be due to a certain amount of sex drive being supplied by adrenal androgens.

The 45 cases under consideration here include both juvenile and young adult types. Thirty-three patients fell into the juvenile age group with an average age of 14 years, while 12 were adults of average age of 27 years.

CASE SELECTION.

In the selection of cases there were two main groups:

(*a*) Those chosen on account of various forms of excessive sexuality, and

(*b*) Those selected on account of signs of excessive activity in other fields, and not considered to be sexual offenders.

(*a*) Some of these were primarily under care in hospital as sexual offenders, others were admitted on account of a generally psychopathic, schizophrenic or neurotic symptom complexes, and sexual disorder formed but a part of the total picture. Oestrogens, usually in the form of stilboestrol, were prescribed for excess of hetero- or homosexuality, with complications such as self mutilation, excess masturbation, castration fantasies and exposure.

Amongst those successfully treated was J. M—, a man aged 32, who was sent to hospital on account of an attempt to enucleate his testes with a razor, resulting in a severe scrotal laceration. This was an impulsive act of exasperation at his continued masturbation for 15 years. His outlook was definitely homosexual, and he was preoccupied in fantasy with homosexual perversions which he does not seem to have actually practised. Apart from this he came from an unsettled home with a mother who was indifferent to him, had a Nonconformist upbringing, and was somewhat obsessional in habits. Superficially he has passed for normal. While in hospital his masturbatory desires began to return, having been temporarily absent after his self-mutilation. Under dienoestrol, mgm. i *t.d.s.*, they subsided, and he declared himself to be less irritable and more cheerful than for years. He was discharged much improved.

(*b*) Stilboestrol was also used in a smaller group of 17 patients *not* associated with any special disorder in the sexual sphere, but who were either predominantly aggressive or anxious.

In the case of E. P—, aged 33, he was an immature man who was subject to periods of tension, his intolerance of which was displayed in bouts of violent temper, headaches, and paranoid feelings towards his mother. He also dreamt of violence going on around him. While in hospital on stilboestrol, mgm. 5–10 daily for five months, he had no outbursts of temper, and was generally improved. He was also treated psychotherapeutically, but it is uncertain how much he benefited from this, owing to his unsympathetic co-operation in this type of treatment.

Trial of stilboestrol was made on several tense, aggressive young schizophrenics without any definite response, though some appeared quieter and more settled during some months on the drug than during an equivalent period without it. Where psychopathic forms of behaviour were associated with an epileptic constitution, or with organic brain disease, no improvement was observed in this series of cases.

To summarize the clinical results:

(1) In a group of 27 psychopathic, schizophrenic and neurotic cases, where stilboestrol was given to control various forms of abnormal sexuality, 10 were considerably improved, 15 improved, and two unchanged.

(2) In the 17 cases treated for alleviation of tension and aggression, without any particular abnormality sexually, nine patients displayed various degrees of improvement and eight showed no change.

Dosage.

The usual method was to start with stilboestrol, mgm. 1 or 2 the first week, according to age and urgency, thereafter raising the dose by mgm. 1 weekly to a maximum of 4 to 9 mgm. weekly. To obtain the necessary effect mentally, it was necessary to maintain a moderate but not excessive degree of gynaecomastic response. Treatment was maintained from one to five months, sometimes with an interval of a week to allow excessive gynaecomastia to subside. No "tailing off" was required.

Mental and Physical Effects.

The mental response was generally evident in from five to ten days after the initial dose, and was characterized by a decreased preoccupation with sexual ideas and activities, normal and abnormal. To use the patients' own descriptions: "The homosexual thoughts were wiped clean," "the dirty thoughts have gone"; "It makes it possible for me to cope with masturbation"; "Controlling homosexual urges most definitely, feel a lot better in myself," etc. With these feelings there was some decrease in activity as a rule.

Physically, the nipples take on a deep brown pigmentation, become enlarged and feel tender or even raw. There is usually a little swelling of the breast tissues around the nipples, and the areola is also pigmented. With the graduated dosage scheme this response has rarely led to cessation of treatment, though an occasional interval is required. The traditional nausea was seen but once, and there has been no vomiting. The onset of physical changes usually correlated with the psychological response.

Change in weight appeared positively correlated with the clinical state, in that gains averaging 10 lb. were associated with improvement in eight patients, losses averaging 5 lb. with poor results or dubious temporary improvement, and a static weight was associated with success and failure equally in eleven others.

Damage to Testes.

Since the use of oestrogens has been advocated as a means of chemical castration, the risk of any permanent cessation of testicular function in the type of case with which this investigation is concerned is important. In relation to this, Golla and Hodge (1949), in observations over six years, found that libido was absent so long as maintenance doses of oestrone were continued. In some of their acromegalic cases, libido returned in two weeks after treatment stopped ; and in another case after four years of oestradiol injections producing absence of libido, intermission of treatment resulted in return of libido in three weeks. In two cases injections of testosterone propionate restored potency even while oestrone was continuing. Their view is that even after years of oestrone treatment there is no reason to believe that sexual power is permanently abolished. None the less, Dunn states that when stilboestrol is administered in large doses, e.g., " 5 mgm. over an extended period " atrophy of the testes results, and the changes in size of the testes are permanent. Later, Dunn does, however, report recovery of spermatogenesis in two sexual perverts in whom it had been completely knocked out by stilboestrol. Bishop (1952), in a small series of males treated for acne, reported that as a result of follow-up he was of the opinion that spermatogenesis recovered fully.

In my own patients, two to five months has been the usual period of continuous treatment. If longer is needed, an interval of a month is desirable.

The Mode of Action.

It is likely that in men, as in women, the luteinizing hormone may only be able to act when primed by the follicle stimulating hormone. The luteinizing hormone has been shown to be identical with the hormone stimulating the interstitial (or Leydig) cells (I.C.S.H.), and this hormone controls the secretion of testicular androgen. If F.S.H. and L.H. are inhibited by a rise in blood oestrin concentration, spermatogenesis and androgen secretion will fall, with a consequent reduction of sexual activity.

There is at least a possiblity that oestrogen may have a direct pharmacological effect on the central nervous system. Zuckerman (1952) has demonstrated, through his experiments on rats, that learning can be influenced by sex hormones, and that oestrogen can act as a cerebral depressant in these rodents. While it has yet to be shown that a similar influence is exerted in humans, there are some indications clinically that performance may be impaired, though more investigation is needed before any conclusion is reached.

The type of male juvenile or adolescent who responds well to oestrogenic therapy is usually immature emotionally, sometimes intellectually and socially also. In these patients oestrogens assist reintegration by controlling urges with which such personalities cannot deal normally, restoring homeostasis as it were. Reduction of excessive sexuality, either actual or relative, is often enough to enable the patient to settle down, with the result that other symptoms such as attacks of rage may also disappear. The process is best initiated with stilboestrol, but should be supported with psychotherapeutic and occupational methods.

The use of stilboestrol has done much to make the treatment of psychiatric states complicated by sexual disorders possible in hospital, and to allow such patients a degree of freedom which would formerly have been too great a risk. It has assisted in enabling one of the provisions of the Criminal Justice Act, 1948, to be carried out, and in our juvenile unit it has been most useful in controlling occasional outbreaks of homosexual behaviour in the 12 to 16 age groups.

Combined Diandrone and Stilboestrol Therapy in Schizophrenia after Insulin Coma Treatment.

It sometimes happens that when the more florid and acute symptoms of schizophrenia have been improved by insulin comas, the patient is left with a residual disability, partly schizophrenic and partly inadequate in character, with lack of initiative, vagueness, inferiority and unsystematized paranoid ideas. Examination of the *pre-morbid personality* usually shows that similar defects have been evident in the patient's earlier social life. The following cases illustrate how endocrines may assist in clearing such residual symptoms.

D. M—, aged 17, was admitted in September, 1951. In childhood he had few friends, kept to himself and was bullied at school. His intelligence was low average, and he had many jobs since leaving school. On admission he felt that he was spied on at home, and that everyone was against him. He said, "They have a system of signs and pass words." Said he was dirt, and yet complained that he was treated as dirt. He had violent aggressive fantasies of killing people, and at times of killing himself. He also talked of incestuous ideas of having been intimate with his younger sister. Castration fantasies were present. The father was strict and idolized the patient's sisters, and it is possible that his incestuous assertions may have sprung from jealousy of his siblings and from revenge on his father. His mood was dull, but it was felt that he might put his aggressive fantasies into practice. After 30 insulin comas and two E.C.T. he was improved. Not only was he less aggressive and paranoid, but apathetic and seemed to be covering up. Incestuous fantasies continued, so he was started on stilboestrol, mgm. 3–6 daily. Ten days later the incestuous thoughts were relieved and he had no desire to kill people, but was still rather apathetic and unstable, lacking confidence and occupationally doing little. To combat these last features, and four months after stilboestrol treatment began, he was also started on diandrone mgm. 20 daily. In two weeks he had become more confident, energetic, working well at the occupations department and mixing better socially. In four to five weeks he had become over-aggressive, and there were signs of paranoid ideas returning.

The diandrone was omitted after five weeks for an interval of three weeks. He lost his tension and was again swinging in the direction of apathy. At this point diandrone mgm. 10 was restarted. In two weeks he was again working, more confident and had lost his former laziness. After another three months he was again losing initiative and activity. To meet this his stilboestrol was reduced to mgm. 2 daily, and the diandrone raised to mgm. 20 daily. On this dosage he was able to be discharged to his home, with out-patient supervision, last November.

This case illustrates quite well the rôle which these various physical methods can play. The grosser disturbance was controlled by insulin comas, while stilboestrol for his sex difficulties, and diandrone for his social adaptation, were used to bring him along to the point of discharge, and to prevent the relapse that at one time threatened him.

In conclusion it is certain that neither diandrone nor oestrogens constitute a treatment for any neurosis or psychosis. These endocrines have a limited but specific action in certain social and sexual fields, as described. They can be used to improve progress with other established forms of psychological and physical treatment. Much remains to be learnt about their use and their biochemical relationships, which are being further studied.

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THE ELECTROENCEPHALOGRAM IN MANIC-DEPRESSIVE PSYCHOSIS.

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The main object of this investigation is to verify the claim of Pauline Davis (1941) that manic-depressive depressed psychotics (M.D.D.s) tend to possess frequencies of alpha rhythm in the E.E.G. at 10 c./sec. or slower, whilst manic-depressive manic patients (M.D.M.s) tend to show alpha frequencies at 10 c./sec. or faster; furthermore that there is no shift in alpha frequency corresponding to change in psychotic phase or in degree of phase. These claims are of importance in relation to a recent paper by Mundy-Castle (1951*b*) in which a significant correlation was reported between ratings of the Heymans-Wiersma temperament variable secondary function and mean frequencies of alpha rhythm in normal adults, since both Heymans (1929) and Wiersma (1932) maintained that M.D.D.s possessed a high degree of secondary function and M.D.M.s a low degree of this variable. To explain this in more detail, secondary function is postulated as being present in individuals in different degrees varying over a continuous scale ranging from domination of the conscious field by secondary function to domination by primary experience (relative lack of secondary function). Individuals displaying the former may be referred to as secondary functioning, their behaviour being characterized by steadiness of action, continuity of interest, evenness of mood and psychic tempo, reduced stimulability and a tendency for mental events to perseverate. Individuals in whom secondary function is relatively lacking (it can never be wholly absent) may be termed primary functioning, their behaviour being characterized by impulsiveness, mobility, high stimulability and a quick and variable psychic tempo. The Heymans-Wiersma temperament scheme has been developed extensively by Biesheuvel (1935, 1949). Mundy-Castle's study revealed that subjects rated as secondary functioning possessed low alpha frequencies whilst those rated as primary functioning possessed high alpha frequencies. The present investigation should help to elucidate the view of Heymans and Wiersma concerning secondary function and manic-depressive psychosis.

Also to be presented will be a detailed analysis of the E.E.G. characteristics found in manic-depressive psychosis and involutional melancholia compared with a normal control group, studying in particular any E.E.G. patterns which are akin to the Davis "choppy" classification. The latter encompasses diffuse or localized, intermittent or permanent, disorganized low voltage fast activity ranging from 26 to over 50 c./sec. It was claimed not to be artifact or muscle activity and was regarded as an abnormal interference with the normal physiological activity of the cortex. In support of this contention, Davis presented evidence that choppy activity is associated with organic pathology (1940, 1942) and with direct chemical stimulation of the cerebral cortex (Davis and Sulzbach, 1940). The choppy pattern was reported to be prominent in the E.E.G.s of schizophrenics (60 per cent.), whilst the figure for manic-depressive psychotics was 39 per cent. (Davis, 1942). It should be stressed that the choppy classification was criticized by Walter (1942) and Hill (Hill and Parr, 1950, ch. ix) who point out that such a pattern might well be due to alpha rhythm inhibition plus attenuated muscle potential artifact, and will be apparent if short time constants such as those of Davis are used.

MATERIAL AND PROCEDURE.

The material of this investigation comprises 165 E.E.G.s recorded from 117 manic-depressive and involutional melancholic patients of Weskoppies Hospital, Pretoria, there being 48 repeats. Their mean age was 54·96 years, standard deviation 14·48 years. The patients were transported by van from Pretoria to the National Institute for Personnel Research, Johannesburg, a distance of about 38 miles, which meant that the first-named author was in their company for two periods of about an hour during the journey, as well as during the test and often at other times of the day. The recordings were carried on for a period of over two years, from 21 April, 1949, to 21 June, 1951. A control E.E.G. study of 160 young normal adults (mean age 22·4 years, standard deviation 5 years) was available for comparison purposes.

Clinical and Psychological Assessment.

A standard classification of manic-depressive psychosis and its sub-groups was adopted. The diagnosis of the condition as manic-depressive psychosis was dependent on the strict conception of the disease, namely, care was taken to exclude: (1) schizophrenics whose psychosis starts with an episode of excitement; (2) cases with persistent hallucinations and ideational dissociation, i.e., schizophrenes; (3) depressions of a reactive or situational nature, which are better classified as psychoneurotic; (4) cases which do not revert to the usual level of affective intensity, integration and dynamics after attacks (allowing for self-protective timidity). The sub-groups employed were as follows:

(1) mania, chronic mania, recurrent mania;

(2) depression, recurrent depression;

(3) alternating, i.e., with normal intervals between psychotic episodes which are of both manic and depressive types;

(4) circular, i.e., episodes of both manic and depressive types running into each other;

(5) attacks of double form, i.e., each psychotic episode comprising a manic and a depressive phase merging into each other but with intervals of normality between each of these double-form attacks. One case only of this type occurred in our series and for statistical reasons it was accordingly grouped with the circular cases.

The standard view of involutional melancholia was adopted rather than the wider concept of involutional psychosis enunciated by Kallmann (1950). Only those cases are included which manifest melancholic mental content for the first time in the involutional period, without impairment of their intellectual functions.

The degree of the mania or depression at the time of the E.E.G. was assessed on a 3-point scale, as follows :

Mania.

Degree 1 (M1) : Hypomania-euphoric and/or aggressive, mildly overactive, talkative in a rapid fashion with a tendency to distractibility and mild flight of ideas.

Degrees 2 and 3 (M2 and M3) : Moderate and gross exaggeration of the features of degree 1, often associated with rapidly changing delusions of grandiose and persecutory types.

Depression.

Degree 1 (D1) : Relatively mildly depressed mood, with mild inhibition or agitation but without delusions of depressed type.

Degrees 2 and 3 (D2 and D3) : Exaggeration of the depressed mood and of the agitation or inhibition of degree 1 (amounting in degree 2 to mild and in degree 3 to profound stupor) and often with overt or indirect evidence of delusions of depressed type.

Our material contained examples of both degrees 2 and 3 depression but none of degree 3 mania for the obvious reason that no such grossly excited case could be transported as described and be submitted to an E.E.G. test. For statistical purposes, therefore, we have decided to group degrees 2 and 3 depression together for the sake of uniformity with the manics so that in both cases there are sub-groups exhibiting a milder and severer degree of the tendency in question.

The problem of what is meant by a mixed phase merits special consideration as there is often a tendency to refer to circular or even alternating forms of manic-depressive psychosis as mixed in view of the fact that both types of phase are represented. In the present study such usage is rejected, the term being used in the strict sense of the co-existence at one and the same time of symptoms characteristic of both the manic and the depressed phase—or at the very least extremely rapid fluctuations within a matter of seconds between manic and depressive features. These states are classified in Kraepelin's standard system under the heads of maniacal stupor, agitated depression, unproductive mania, depressive mania, depression with flight of ideas and akinetic mania. Henderson and Gillespie (1944) regard all of these, but for agitated depression and sometimes maniacal stupor, as transition phases between manic and depressed attacks.

Insight into the composition of such mixed states may be obtained by regarding them as mixtures of varying degrees of the three psychological components :

(1) mood, elated or plus, inhibition or minus ;

(2) motility, overactivity or plus, inhibition or minus ;

(3) psychic tempo, as revealed in rapid talk with distractibility and flight of ideas rated as plus, or in retardation of speech and varying degrees of inaccessibility rated as minus. Accordingly we have rated all our cases at the time of the test as plus or minus on each of these components.

In addition to a clinical and psychological assessment of each case at the time of the test, an assessment was made on the basis of a thorough study of the case record as to whether the manic or depressive phases were predominant or whether they were equal.

Thus, to summarize our salient psychiatric data to appear in the statistical analysis, as regards the phase at the time of the test, cases were classified as (1) manic, (2) depressed, (3) normal, (4) mixed, and as regards the predominant phase of the case as (1) manic, (2) depressed, (3) manic = depressed. Distribution of the psychotic material is presented in Table I.

TABLE I.—*Distribution of Psychotic Material According to Predominant Phase.*

	Manic.	Depressed.	Manic-depressed.	Totals.
Involutional melancholia	0	18	0	18
Recurrent chronic, plain mania	25	0	0	25
Recurrent, chronic, plain depression	0	17	0	17
Alternating	12	2	9	23
Circular	20	7	7	34
Totals	57	44	16	117

Our psychiatric and psychological assessment of every case was checked by a review of the case at the end of the project. There was, moreover, a precaution against subjective bias in diagnosis in that no case was included in our series where the diagnosis of manic-depressive psychosis or involutional melancholia had not also been made independently by the doctors' conference of Weskoppies Hospital (average size of conference 7–8 doctors, approximately half of whom can lay claim to senior psychiatric experience).

E.E.G. Recording Procedure.

A six-channel standard Ediswan E.E.G. was used, together with an Ediswan Walter type frequency analyser for the later recordings. Silver-silver chloride saline pad electrodes were secured to the head by a rubber and whalebone cap, and the standard bipolar electrode combinations were as follows :

(i) fronto-parietal, parieto-occipital, parieto-temporal left and right hemispheres ;

(ii) fronto-temporal, temporo-occipital, parieto-temporal, left and right hemispheres.

Whenever an abnormal focus was noted, detailed spatial analysis was employed. The majority of cases were tested whilst lying supine on a couch with a head-rest designed to exclude interference with the electrodes. As the subjects were mental patients a few cases were too resistive or otherwise-uncooperative for this position and were tested whilst seated. Paper speeds of 1·5 and 3 cms./sec. were both used on all patients, in some cases 6 cms./sec. in addition. In all cases an adequate sample of the record was made with high frequency filters set to cuts of 15 per cent. down at 75 cycles, whilst the standard time constant setting was 0·3 sec. Each recording lasted for a minimum of 8 minutes, during which time study was made of E.E.G. changes during eye opening and closure, 3 minutes' hyperventilation (when possible) and rhythmic photic stimulation with a Scophony electronic stroboscope. Full details of administration of the latter have been given by Mundy-Castle in an earlier paper (1953).

The interval between the E.E.G. and the time of the last meal was also noted, as the degree of starvation or satiety, as reflected notably in the blood-sugar level, is known to affect the E.E.G., particularly during hyperventilation.

The interval between the E.E.G. and shock therapy and the extent of the course of shock treatment were also recorded in every case with a view to assessing the extent to which abnormalities in the records might be referable to such shock therapy. The consensus of opinion is that with E.C.T. such changes disappear in 2 to 3 months (e.g., Kennard and Willner, 1948), but but Mosovich and Katzenelbogen (1946) claim to have detected signs of cerebral dysrhythmia as long as 10 months after treatment. McNeel *et al.* (1941) and Hoagland *et al.* (1937) agree that disturbances introduced into the E.E.G. by high dosage insulin are short-lived.

The E.E.G. concepts employed correspond to those of the British school of Walter and Hill (Hill and Parr, 1950), and include alpha (8–13 c./sec.), beta (14–30 c./sec.), theta (4–7 c./sec.) and delta (1–3·5 c./sec) rhythms. Alpha rhythm is additionally defined as of occipital or parieto-occipital origin and showing attenuation during visual and sometimes mental attention. Alpha activity is also described in terms of responsiveness according to the work of Golla, Hutton and Walter (1943): three classifications are used, (1) R or responsive, showing a normal blocking response; (2) P or persistent, showing little or no blocking response; and (3) M or minus, where alpha rhythms are of low voltage and rarely present. These types have been shown to be related to differences in mental imagery, with M type rhythms being associated with predominantly visual imagery, R types with visual and other imagery equally, and P types with non-visual imagery (see also Short, 1951).

Finally, the records were rated as normal, questionably normal or abnormal, these classifications being based on the criteria of abnormality laid down on pp. 379 and 380 of Hill and Parr (1950).

RESULTS.

1. *Alpha Frequency and Psychotic Phase.*

An association between fundamental psychiatric and psychological features on the one hand and the alpha rhythm on the other was demonstrated, viz., that the manic phase with its positive rating of mood, motility and psychic tempo is associated with relatively high alpha frequency, and that the depressed phase with its negative ratings on the same three psychological variables is associated with low alpha frequency (see Tables II and III).

This is true of:

(*a*) predominant phase;
(*b*) phase at test, which may be a reflection of (*a*).

There were no other significant differences or associations in E.E.G. characteristics corresponding to psychotic phase.

TABLE II.—*Significance of Differences in Alpha Frequency According to Psychotic Phase.*

	Manic.			Depressed.			Critical ratio.	Probability.
	Mean.	S.D.	N.	Mean.	S.D.	N.		
Alpha frequency predominent phase (c/s)	10·36	1·09	54	9·74	0·89	42	2·95	<0·005 significant
Alpha frequency phase at test (c/s)	10·21	1·16	41	9·58	0·86	37	2·71	<0·01 significant

TABLE III.—*Association between Alpha Frequency and Psychotic Phase.*

	Predominant phase.		Phase at test.	
	Manic.	Depressed.	Manic.	Depressed.
Above mean alpha frequency	31	9	23	7
Below mean alpha frequency	23	33	18	30
	$X^2 = 12·58$ $P < 0·001$ significant		$X^2 = 11·36$ $P < 0·001$ significant	

It is *not* true of change of phase or change of degree of phase in the same individual at different tests. This was checked as follows: degrees of depression and mania were rated on a three-point scale, D1, D2, D3 and M1, M2, M3, in order of increasing severity. In assessing the shift of phase the following scale was therefore employed: D3–D2–D1–0–M1–M2–M3. Shift to the right was rated plus and to the left minus. One-step, two-step and three-step shifts were compared *inter se*, and as a combined group they were compared with the group of cases that had shown no shift between tests, to ascertain the degree, if any, of quantitative changes in E.E.G. characteristics, notably alpha frequency. No significant differences or associations were found in this statistical analysis.

2. *Low Voltage Fast Irregular E.E.G.s, Choppiness.*

A special study of low voltage fast irregular records was undertaken as an extension of the Davis choppy classification. After careful analysis of our E.E.G. data it was decided to discard the classification "choppy" and in its place use the following sub-classifications of low voltage fast irregular (l.v.f.i.) records :

Type l.v.f.i.A.—Records showing low voltage rare or intermittent alpha activity considerably disturbed by low voltage fast rhythms ranging from 14–30 c./sec. of a diffuse nature. Some intrusion of low voltage diffuse theta activity is sometimes apparent.

A variant of the above manifesting itself in the form of flat E.E.G.s was originally treated as a separate type designated as l.v.f.i.C. After careful consideration with the aid of frequency analysis these records were reclassified as l.v.f.i.A., the "flatness" being attributed to asynchrony of random high frequency components. Examples of l.v.f.i.A. type records are shown in Fig. 1*a* and *b*.

Davis's choppy activity may be regarded as a variant form of l.v.f.i.A., but with a higher frequency of the fast activity than that designated in our definition. Only 2 of these were found in our material, an example being shown in Fig. 1*c*.

Type l.v.f.i.B.—Records showing excessive diffuse theta activity of medium voltage combined with typical l.v.f.i.A. characteristics. Alpha activity is sometimes of rather higher amplitude than in the l.v.f.i.A. type however (see Fig. 2).

Borderline l.v.f.i.A. and l.v.f.i.B. types.—Those records in which the characteristic activity is less clear and often showing a relatively well-formed though intermittent alpha rhythm.

The incidence of these record types was compared with that in the control group of 160 normal adults. Statistical analysis revealed that when the borderline l.v.f.i.A. and l.v.f.i.B. records are added to the true l.v.f.i.A. and l.v.f.i.B. records there is a significantly higher incidence of l.v.f.i.A. and l.v.f.i.B. records, both separately and combined, in the psychotic group than in the control group. When the borderline groups are treated separately the significant difference persists in the case of l.v.f.i.A., borderline l.v.f.i.A. and borderline l.v.f.i.B. groups, but not with the l.v.f.i.B. records. These figures are shown in Table IV. There were no significant differences in the incidence of any of these low voltage fast irregular records between the predominantly manic and the predominantly depressed sub-groups.

TABLE IV.—*Comparison of Incidence of L.V.F.I. E.E.G.s in the Psychotic and Normal Groups.*

Type of l.v.f.i. E.E.G.	Psychotics.		Normals.		Critical ratio.	Probability.	Whether significant.
	Incidence.	Percentage.	Incidence.	Percentage.			
L.v.f.i.: A	21	17·95	15	9·37	2·03	<0·05	Yes
L.v.f.i.: B	14	11·97	10	6·25	1·60	>0·05	No
Borderline A	18	15·38	8	5·00	2·77	<0·01	Yes
Borderline B	12	10·26	0	0	3·66	<0·001	,,
L.v.f.i.: A + Borderline A	39	33·33	23	14·37	3·67	<0·001	,,
L.v.f.i.: B + Borderline B	26	22·22	10	6·25	3·72	<0·001	,,
All l.v.f.i. records	66	56·41	33	20·62	6·40	<0·001	,,

To test the significance of the age factor the incidence of these types in those psychotics above and below 55 years of age was checked. No significant differences were found.

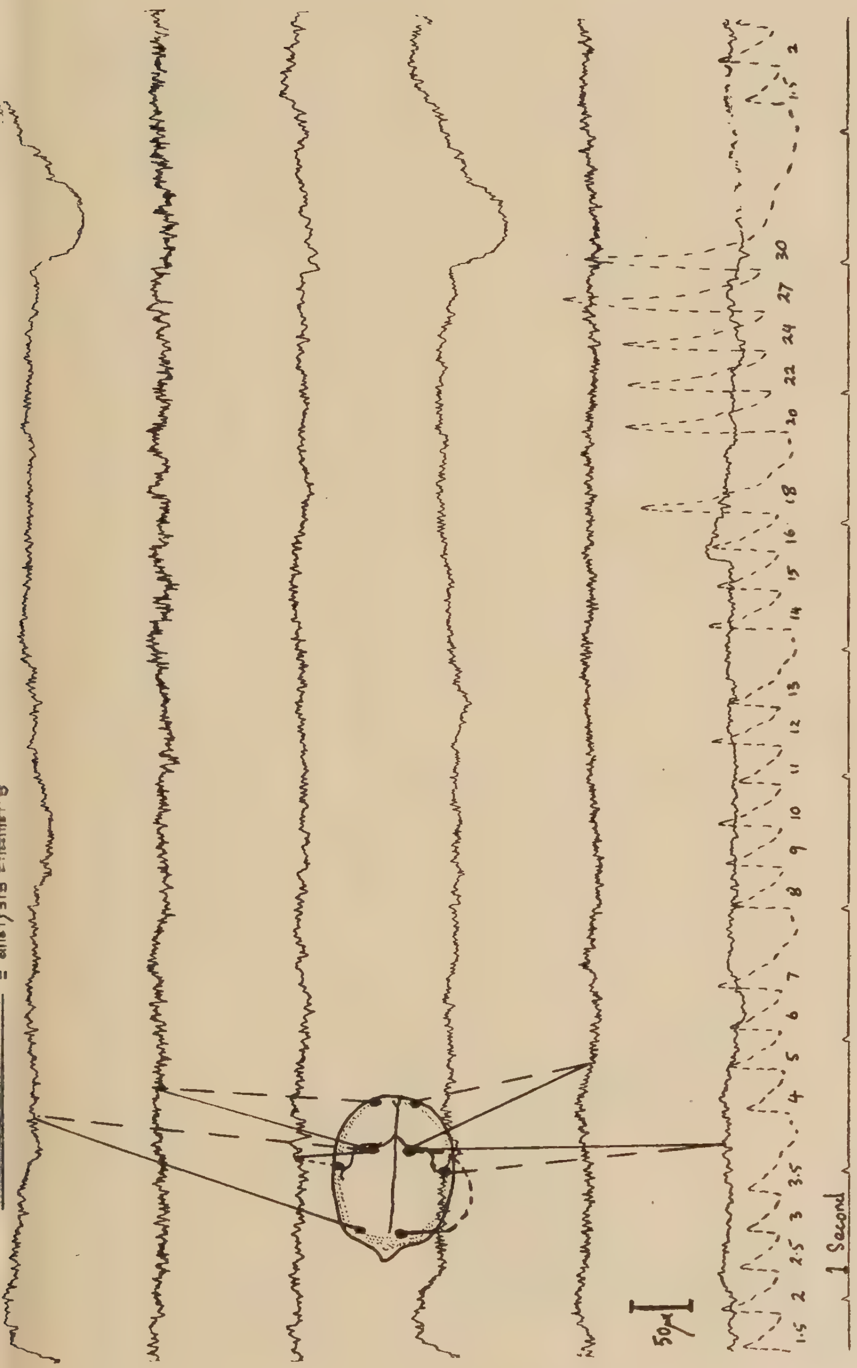


FIG. 1 (*a*).—L.v.f.i.A. record from predominantly depressed patient. Note characteristic frequency spectrum with fast activity dominant, little or no alpha rhythm. (*b*) L.v.f.i.A. record from predominantly manic patient, showing more theta rhythm than in Fig. 1 (*a*). The spikes from channel 6 are of muscular origin. (*c*) Typical Davis "choppy" E.E.G. from predominantly depressed patient. Such an E.E.G. is considered to be a variant of the l.v.f.i.A. classification. Frequencies of fast activity up to 36 c/sec.

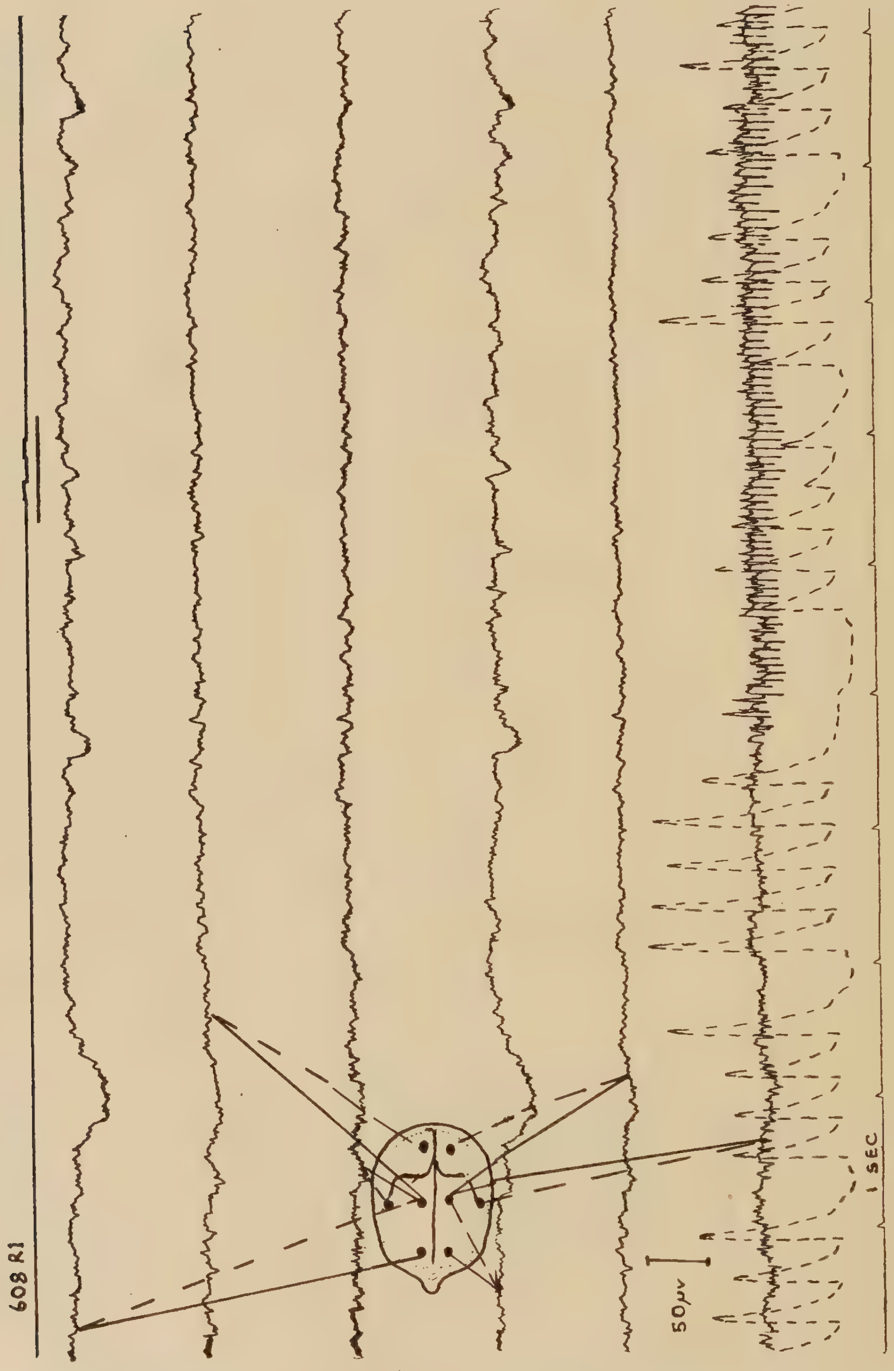


FIG. 1 (*b*).

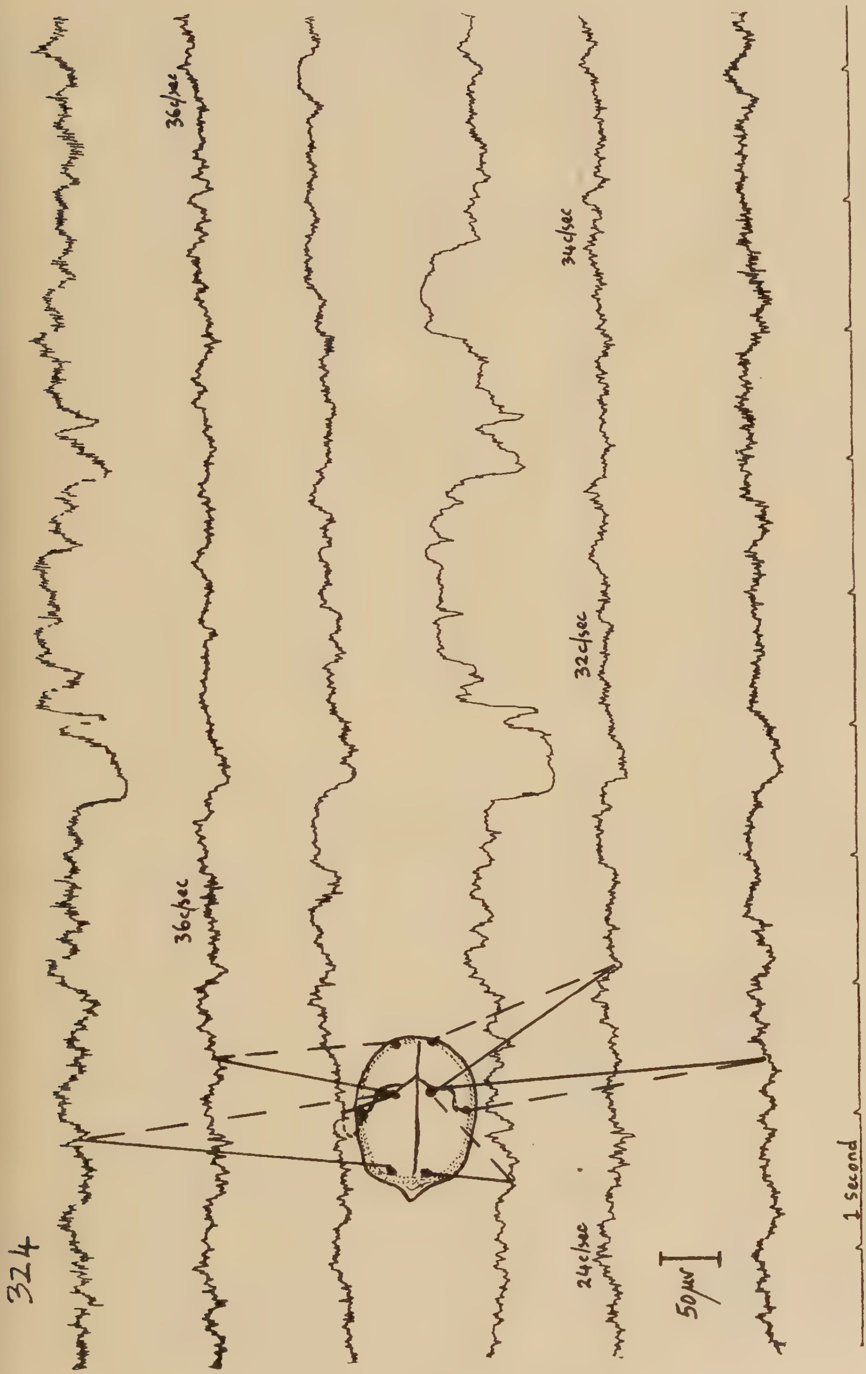


FIG. 1 (c).

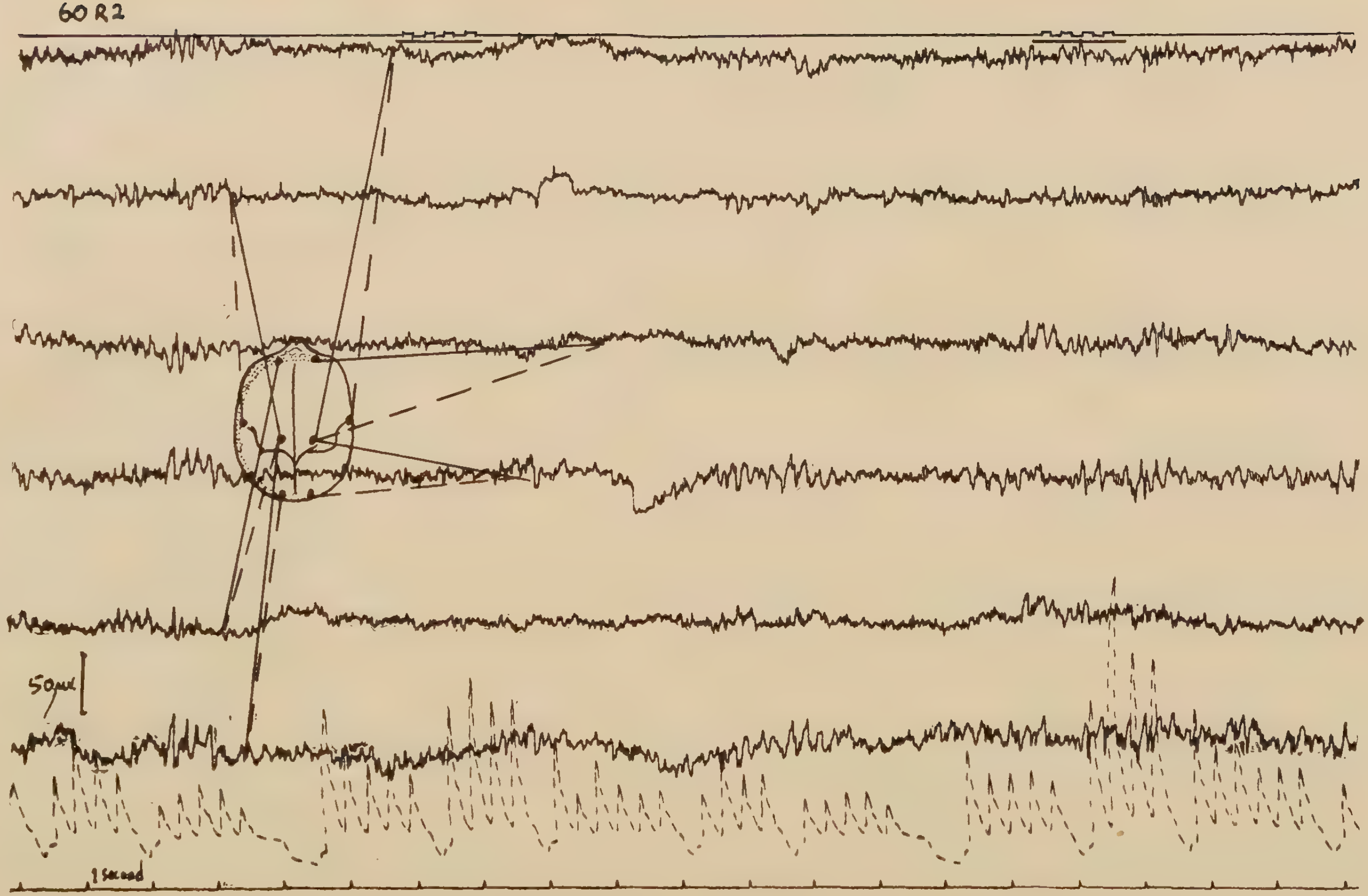


FIG. 2.—L.v.f.i.B. record from involutional melancholic patient. Note excessive theta rhythm combined with l.v.f.i.A. characteristics.

3. *Incidence of Abnormality.*

There were 28 (24 per cent.) abnormal E.E.G.s in the total psychotic group, this being significantly different from the incidence in the normal control group (10 per cent. abnormal; $p < 0{\cdot}01$). The incidence of questionably normal E.E.G.s was also significantly higher, being 25 (21 per cent.) as opposed to 11 per cent. ($p < 0{\cdot}05$).

The influence of age on the normality or otherwise of the E.E.G. was again checked, in view of the fact that about half of our psychotic material falls in the age group 55 years and over, where arteriosclerotic and senile brain changes may affect the E.E.G. Statistical analysis revealed no significant differences in the incidence of questionable or abnormal records between the age groups above and below 55 years of age.

Similar care was taken to evaluate the possible disturbing effects of E.C.T. on the E.E.G. As the estimates of post-E.C.T. disturbances vary from 6 weeks to nearly a year, in our study untreated cases were grouped with cases treated over a year before testing, and compared with cases treated within one year before the test. There were no significant differences.

4. *Comparison of E.E.G. Characteristics with Normal Control Group.*

Statistical details are shown in Table V. It should be noted that the mean age of the psychotic group is significantly greater than that of the control group (CR $= 26{\cdot}50$, $p < 0{\cdot}001$). The following are the salient results:

(i) *Alpha Characteristics.*

(*a*) Mean alpha frequency is significantly lower in the psychotic group.

(*b*) Mean alpha amplitude is significantly lower in the psychotic group.

(*c*) Mean per cent. time alpha is significantly lower in the psychotic group.

(*d*) There was no significant difference in distribution of R, P and M alpha types between the psychotic and normal groups.

(ii) *Beta Characteristics.*

(*a*) Mean beta frequency is significantly higher in the psychotic group.

(*b*) Mean beta amplitude just fails to be significantly higher in the psychotic group (p approx. $0{\cdot}06$).

(iii) *Theta Characteristics.*

Theta amplitude is significantly higher in the psychotic group.

(iv) *Beta and Theta Incidence.*

The incidence of beta rhythm is significantly higher and of theta rhythm significantly lower in the psychotic group.

5. *Flicker Response Characteristics.*

All aspects of responses to rhythmic photic stimulation were compared with those from the normal control group. The figures derived from the latter

TABLE V.—*Comparison of Spontaneous E.E.G. Characteristics: Psychotic and Normal Groups.*

E.E.G. variable.	Psychotics. Mean.	S.D.	N.	Normals. Mean.	S.D.	N.	C.R.	Probability.	Whether significant.
Alpha frequency (c./sec.)	10·04	1·12	112	10·32	0·98	160	2·15	<0·05	Yes
Alpha amplitude (μv.)	24·37	15·85	112	31·99	20·93	160	3·25	<0·001	,,
Per cent. time alpha	43·70	30·18	112	56·10	31·09	160	3·28	<0·001	,,
Beta frequency (c./sec.)	18·98	3·30	86	17·93	3·03	85	2·15	<0·05	,,
Beta amplitude (μv.)	10·85	8·72	86	8·74	5·14	85	1·92	>0·05	No
Theta amplitude (μv.)	22·88	13·28	47	16·60	11·91	105	2·90	<0·01	Yes

have been presented earlier by Mundy-Castle (1953) together with an analysis of the factors contributing to their occurrence and suggestions concerning the origin of individual differences. In the present study we will give only those figures which are significantly different from the control group.

(i) *Flicker following.*—The mean amplitude of responses to flicker over the 4–20 f./sec. range was significantly greater than in the control group, but not in the 21–26 f./sec. range (see Table VI).

TABLE VI.—*Comparison of Mean Flicker Response Amplitudes: Psychotic and Normal Groups.*

Frequency (c/sec.).	Psychotics. Mean amp. (μv.).	S.D.	Normals. Mean amp. (μv.).	S.D.	Critical ratio.	Probability.	Whether significant.
Theta: 4–7	17·19	15·78	12·64	10·01	2·62	<0·01	Yes
Alpha: 8–10	21·46	15·79	13·68	11·90	4·28	<0·001	,,
Alpha: 11–13	22·53	16·20	16·28	12·28	3·35	<0·001	,,
Beta: 14–20	13·99	13·16	10·80	7·80	2·23	<0·05	,,
Beta: 21–26	10·60	12·06	9·07	8·03	1·14	>0·05	No

(ii) *Harmonically related responses.*—There were no significant differences in the incidence of second and third harmonics, nor second and third subharmonics, although the latter (third subharmonics) bordered on significance at the 10–5 per cent. level, since 31 per cent. psychotics showed third subharmonics as opposed to 9 per cent. normals.

(iii) *Abnormal responses.*—There were 7 per cent. abnormal and 5 per cent. questionably normal responses to flicker in the psychotic group. Neither of these figures is statistically significantly greater than in the control group, although both are larger (control incidence was 3·90 per cent. A, 3·25 per cent. ? N).

A qualitative analysis of the nature of abnormal responses revealed that 5 of the 9 were in the frontal spike category (1 of these being associated with initial wave-spikes), 2 showed generalized spike bursts with occasional slow spike wave complexes, 1 was a pure wave-spike response and 1 fell into the dysrhythmic category. Only 2 of these 9 subjects with abnormal flicker responses possessed abnormal resting E.E.G.s. Frontal spikes were accompanied either by jerks or twitches, 2 of them by laughter in addition (both of the latter being D–D2 at the time of recording). Two others showed signs of acute emotional distress. Two subjects with a frontal spike response exhibited complete adaptation after several initial evoked abnormalities, one of these showing a recurrence of evoked abnormalities during a repeat E.E.G. one year later, when there was no adaptation. Another subject showed an abnormal response (frontal spike) only on a second recording twenty-two months after the first, during which time there was a phase change from 0 to D1. An example of an abnormal flicker response from a manic-depressive patient is shown in Fig. 3.

(iv) *Intra-group differences.*—The following differences between the predominantly manic and predominantly depressed groups were tested for significance:

(*a*) Incidence of second and third harmonics of the stimulus frequency in the flicker response pattern.

(*b*) The occurrence of flicker following in the beta range (14–20 c./sec.). When second and third harmonics were considered separately the differences were not significant, but when treated together, the manic group showed a significantly greater incidence of harmonics (manic= 91 per cent., depressed = 71 per cent., C.R. = 2·32, $p < 0{\cdot}025$). The manic group also showed a significantly greater occurrence of flicker following in the beta range than did the depressed group (manic = 75 per cent., depressed = 54 per cent., C.R. = 2·14, $p < 0{\cdot}05$).

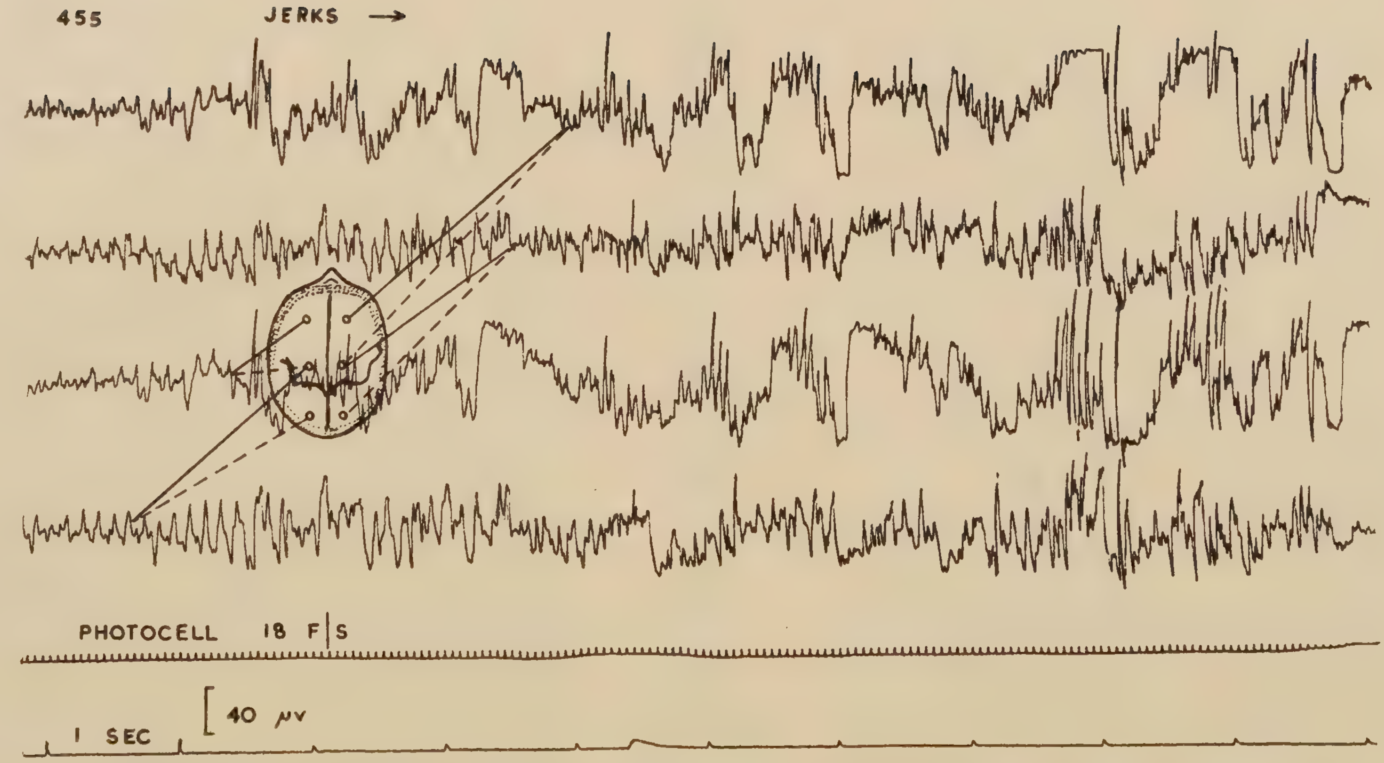
6. *Hyperventilation.*

There were no distinctive features relating to responses to hyperventilation among the psychotic group. Seven subjects revealed an augmentation of existing abnormalities, and no subjects with a normal resting record showed an abnormal response.

DISCUSSION.

The results of this investigation confirm the report of Davis that there is a relationship between alpha frequency and predominant psychotic phase in manic-depressive psychosis, and that there is no change in alpha frequency with shift in phase.

We have already alluded to the report by Mundy-Castle (1951) of a relationship between alpha frequency and ratings of the Heymans-Wiersma temperament variable secondary function. Both Heymans and Wiersma maintained that the poles of the manic-depressive continuum are comparable to extremes of the primary-secondary function continuum, and that the two continua are comparable. The present findings do not support this contention, since change of phase in the individual manic-depressive is not accompanied by a shift in alpha frequency. This is not surprising, however, since the diagnoses "manic" or "depressed" are probably determined as much by assessments of mood and motility as by psychic tempo, which is the clinical variable most likely to be related to primary-secondary function. It therefore seems invalid to regard mania and depression simply as extremes of primary and secondary function. The most likely hypothesis to explain our finding of the importance of predominant clinical phase as the determinant of mean alpha frequency is that this predominant phase indicates a basic temperamental factor, i.e., degree of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1 SEC

FIG. 3.—Abnormal flicker response from involutional melancholic patient. Note build-up of occipital second subharmonic, to break down into slow irregular activity followed by frontal spikes and jerks. Some of the later abnormalities are generalized.

secondary function, and that swings towards the opposite phase are brought about by some extraneous factor or process. If this is so, the view that mania and depression are extremes of primary and secondary function should be discarded, since apart from the absence of change in alpha frequency with change in phase, there is no predominance of very high or very low alpha frequencies in the psychotic group, nor is there a significantly greater scatter about the mean than in the control group. In support of the hypothesis that predominant psychotic phase is related to the secondary function temperament variable are the results concerning differences in flicker response characteristics between the predominantly manic and predominantly depressed groups. In this analysis the former group showed a significantly greater incidence of harmonics and a significantly greater incidence of flicker following in the 14–26 c./sec. range than the latter. The implications of these findings accord with the report of Mundy-Castle (1953) that among normal subjects there are significant associations between alpha frequency, the occurrence of harmonics during flicker, and the occurrence of flicker following in the 14–26 c./sec. band: subjects with high alpha frequencies displayed a significantly greater incidence of second and third harmonics during flicker and a significantly greater occurrence of flicker following in the 14–26 c./sec. band than did subjects with low alpha frequencies. It was postulated that these differences, together with the apparent relationship of alpha frequency to degree of secondary function, are attributable to differences in excitability within the central nervous system, i.e., that primary functioning subjects possess higher excitability characteristics than secondary functioning subjects. Evidence of a different kind in support of this view has been provided by Heymans (1929), Wiersma (1932), Biesheuvel (1938) and Mundy-Castle and McKiever (1953). Gastaut *et al.* (1951) appear to have provided further supporting evidence, for although these workers did not invoke the secondary function concept, the terms they used to describe behavioural differences corresponding to different levels of cortical excitability are clearly very similar to those connoted by primary-secondary function. In view of the foregoing considerations it is proposed that similar differences are present among manic-depressive psychotics, namely that levels of central nervous excitability are higher among predominantly manic than predominantly depressed subjects. On this view, the former are likely to possess primary functioning temperaments and the latter secondary functioning temperaments.

The remaining consideration is that of the significantly greater incidence of low voltage fast irregular E.E.G.s in our manic-depressive and involutional melancholia group when compared with the normal control group. Further research is necessary to establish the significance of this type of E.E.G., but in the meantime a possible explanation for its predominance in our psychotic group is that it reflects the effects of an intermittent physico-chemical disturbance of cortical cells brought about by attack by a chemical noxa, probably of endocrine type. This hypothesis has been presented in detail by Hurst (1952*b*) and is an extension of a hypothesis evolved by Kallmann (1938, 1950) for schizophrenia, and elaborated by Hurst (1950, 1952*a*) for the same disease. In support of such a toxic-organic view of manic-depressive psychosis, Hurst

(1952*b*) cites in particular the neuropathological findings based on human biopsy material as well as animal experimentation of Penfield and Cone (1926), Elvidge and Reed (1938), Cardona (1934) and others. The most significant observation derived from these studies is acute swelling of oligodendroglia found in manic-depressive psychosis, schizophrenia, organic brain disease and epilepsy, but not in patients who are mentally normal. This pathological process was found to occur at any depth in the white matter between the grey matter of the cortex and the ventricle, perhaps more prominent at a depth of 1 cm. and in the deeper layers. It may be patchy or generalized. Also of relevance are the reports of Rupp and Wilson (1949) and Papez and Bateman (1949) describing cortical degenerative changes in groups of psychotic patients among whom were a total of 17 manic-depressives and 2 involutional melancholics. The majority of the remainder in these two studies were schizophrenics (62).

Taking these findings in conjunction with the type of evidence offered by Davis to explain her " choppy " E.E.G.s, in particular that choppy activity is associated with organic pathology and with direct chemical stimulation of the cortex, it is possible that the l.v.f.i. predominance in our psychotic group reflects such a toxic-organic pathogenesis of manic-depressive psychosis, although clearly such a hypothesis can only be tentative.

In view of the predominance of rare intermittent and low voltage alpha rhythms in the l.v.f.i. E.E.G.s, a check was made on the possible rôle of attention in producing this kind of record by comparing the incidence of l.v.f.i.A and l.v.f.i.B records in manic and depressed cases, both in terms of predominant phase and phase at test, since these phases contrast psychologically and particularly in attention. No significant differences were found.

The significantly greater incidence of abnormal and questionable E.E.G.s in the psychotic than in the control group might be construed as further support for the toxic-organic view, but it must be remembered that the psychotic group has a significantly higher mean age than the control. We have established that in normal seniles the incidence of abnormality is far greater than in young normal adults (our figure for 50 normal seniles with a mean age of 75 years was 26 per cent.(Mundy-Castle *et al.*, 1953), so that the significance of the abnormality incidence in the psychotic group is not wholly clear. The lack of a significant difference between the under and over 55 year age groups suggests, however, that the greater incidence of abnormality among the psychotics is not solely due to an ageing process.

It is interesting to note that there is a significantly greater mean amplitude of flicker following in the 4–20 c./sec. range among the psychotic than in the control group. We had noticed before the statistical analysis that amplitudes of flicker following were often large in the psychotic group, a typical example being shown in Fig. 4. As yet no reason can be given for this difference from normals, unless it is related to an attention factor, e.g., that the psychotics pay less attention to the stimulus than the normals, thereby permitting a greater degree of synchronization of the cortical cells participating in the response pattern.

The remaining significant differences in E.E.G. characteristics between

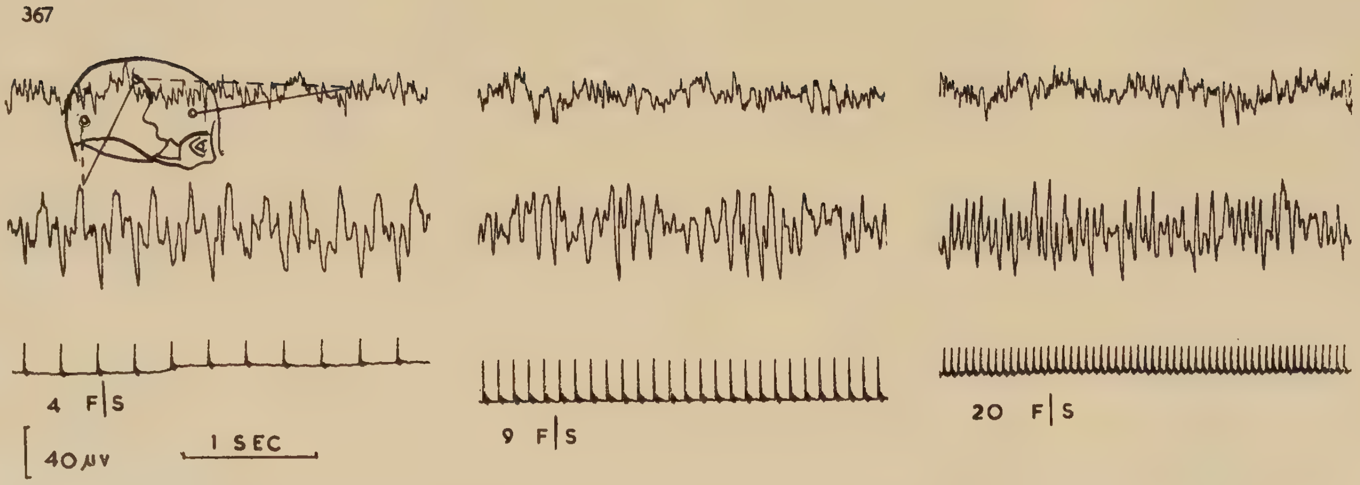

Fig. 4.—High voltage flicker responses from predominantly depressed patient. Note how the high amplitudes of response are maintained at both low and high frequencies. High amplitudes of flicker response are common amongst manic-depressive psychotics.

the psychotic and control groups are explicable in terms of the age factor and that contributing to the occurrence of l.v.f.i. records. Alpha frequency, amplitude and per cent. time all decrease with age (Mundy-Castle *et al.*, 1953) whilst the last two are by definition less prominent in l.v.f.i. records. Incidence of theta rhythm decreases with age whilst its amplitude increases, suggesting a different kind of theta rhythm, probably related to the increased incidence of abnormality (Mundy-Castle, 1951*a*). The significantly higher mean beta frequency and greater incidence of beta rhythm among the psychotics can be attributed to the difference in incidence of l.v.f.i. E.E.G.s.

SUMMARY.

1. The E.E.G.s of a group of 117 manic-depressive and involutional melancholic patients (mean age 55 years) were analysed. Forty-eight patients were given repeat E.E.G.s. A control group of 160 normal adults (mean age 22 years) was available for comparison. The following are the salient results:

   (*a*) There were associations between cases with a history of predominantly manic phase and relatively high frequency of alpha rhythm, and cases with a history of predominantly depressed phase and low alpha frequency.

   (*b*) There was no shift in alpha frequency corresponding to change in psychotic phase or change in degree of phase.

   (*c*) There were significantly more low voltage fast irregular E.E.G.s among the psychotics than the normal subjects. This did not appear to be related to age.

   (*d*) There were significantly more abnormal (24 per cent.) and questionable (21 per cent.) E.E.G.s among the psychotics than the normals. The age difference may contribute to this finding.

   (*e*) Predominantly manic patients showed a significantly greater incidence of second and third harmonics and of following in the 14–26 c./sec. band in their flicker response patterns, than did predominantly depressed patients.

2. The relationship between alpha frequency and predominant phase in manic-depressive psychosis is attributed to differences in degree of the basic temperamental variable secondary function. The differences in flicker response characteristics between predominantly manic and predominantly depressed cases support this hypothesis together with the postulate that secondary function is related to levels of excitability within the central nervous system. It is suggested that subjects who are primary functioning and develop manic-depressive psychosis are more likely to be manic than depressed; conversely, subjects who are secondary functioning are more likely to be depressed than manic. Changes in phase are attributed to an extraneous factor or process.

3. The possibility that the high incidence of low voltage fast irregular E.E.G.s in the psychotic group is related to a toxic-organic pathogenesis of manic-depressive psychosis is discussed. Such a view can only be tentative and verification is dependent on future research.

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CHANGES IN DURATION OF STAY OF MENTAL HOSPITAL PATIENTS SUFFERING FROM FUNCTIONAL PSYCHOSES DURING THE PAST 20 YEARS.

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WE have reported a follow-up study of patients first admitted to London County Council Mental Hospitals in 1930 (Harris and Lubin, 1952, Harris and Norris, in press). The present paper deals with a group of similar patients, i.e., psychotics from whom epileptics, known organic cases, ascertained mental defectives, those over the age of 40 and those who had been admitted to a mental hospital previously were excluded, who were transferred to mental hospitals from St. Francis Observation Ward during the period May 1940 to May 1942. The main differences between this group and the 1930 one were: (*a*) The Mental Treatment Act of 1930 had come into operation and many were admitted to mental hospitals as voluntary patients; (*b*) modern physical methods of treatment were in use; (*c*) in most cases the history was known.

The patients were all under the care of one of the authors (A. H.) for approximately a fortnight in St. Francis Hospital. A generally acknowledged effect of the Mental Treatment Act has been the admission to mental hospitals of less severely ill patients than formerly. However, this tendency is likely to be less marked in the present series of patients, who had all been through the observation ward, than in the total of mental hospital patients, many of whom are admitted on a voluntary basis direct from outpatients clinics and general hospitals. Many of the patients in this series were not certifiable and would have had to be discharged if they had refused voluntary treatment, but on the other hand some of the voluntary patients were certifiable and would have been so dealt with if they had proved unco-operative.

The follow-up of the present series of 200 patients was carried out during 1951, by a search of the hospital records and of those of the Board of Control as before. It was decided, however, to omit the search of the Register of Deaths, since in the previous investigation this proved extremely laborious and costly and very few patients were found to have died out of mental hospitals, it being clear that the mortality rate among ex-mental hospital patients living in the community is no greater than that among the general population. 89 patients, or 44·5 per cent., were traced completely through the hospital records and in 22 of the remainder 11 per cent. of the total, further evidence of subsequent hospitalization was obtained from the files of the Board of Control, leaving 89, or 44·5 per cent., who were deemed to have kept out of mental hospitals since their last recorded discharge, the corresponding figures in the previous follow-up being 50 per cent., 9 per cent. and 40 per cent. The slight fall in the proportion of patients completely traceable through the mental hospital records is probably related to the rise in the proportion of patients whose stay in hospital was comparatively brief.

COMPARISON OF RESULTS.

Hereafter the patients first admitted to mental hospitals in 1930 are referred to as Group A and those first admitted to mental hospitals in 1940/42 as Group B. The composition of these two groups with respect to age and diagnosis is given in Table I. There are some differences, statistically insignificant, between the groups, which may therefore be regarded as similar in these respects. The overall death rate for period A was 10·1 per cent. and for B 6·5 per cent.; the difference is not significant (*P* is greater than ·10). In the ensuing figures the deaths have been omitted.

TABLE I.—*Comparative Distribution of Patients in Periods A and B by Age and Diagnosis.*

	Number of patients.			
	A		B	
Diagnosis and age.	Observed.	Expected.	Observed.	Expected.
Schizophrenia—				
Less than 20 years	50	51·65	18	16·35
20–29 years	187	172·43	40	54·57
30–39 ,,	120	126·85	47	40·15
Affective disorder—				
Less than 20 years	17	18·99	8	6·01
20–29 years	53	56·97	22	18·03
30–39 ,,	98	93·43	25	29·57
Atypical disorder—				
Less than 20 years	15	13·67	3	4·33
20–29 years	55	56·21	19	17·79
30–39 ,,	37	41·78	18	13·22
Total	632	631·98	200	200·02

Chi square = 12·75 *P* is greater than 0·10.

Whereas all the patients in Group A were certified, in Group B 38 per cent. were voluntary throughout their stay in mental hospital, 37 per cent. were certified throughout, and 25 per cent. were admitted initially under one status which was changed either in the same or in a subsequent admission to another status. Of those patients who were only admitted once in the follow-up period of ten years, 55·7 per cent. were voluntary all through their stay, 30·9 per cent.

were certified and 13·4 per cent. had changed from one status to another, usually from certification on admission to voluntary status. The readmission rate in period A was 15·8 per cent. and in B 29·4 per cent.; this difference is highly significant (*P* is less than ·001).

In Group B 27 per cent. of the patients remained in hospital throughout the whole of the first 10 years, the corresponding figure for Group A being 43 per cent., so that there is in Group A an excess of observed over expected cases with a stay of a full ten years.

However, of the certified patients in Group B 54 per cent. stayed the full ten years. 44 per cent. of the Group B patients had only one admission which terminated by discharge in the follow-up period, compared with 41 per cent. in the case of the Group A patients, so that the observed number of patients having only one admission in both groups correspond closely with the expectation. In B 63 per cent. of those who had only one admission were voluntary patients. A comparison by numbers of admissions (Table II*a*) shows significant differences (Chi square = 24·3; d.f. = 3; *P* is less than ·01) there being an excess in Group B of patients having two or more admissions and an excess in A of patients staying throughout. If we take certified patients in Group B alone, however, we find no significant differences between them and Group A (Chi square is less than 7·815; d.f. = 3; *P* is greater than ·05).

Table II (*b*) gives details of the time spent in hospital by those patients who were admitted only once. Comparing Groups A and B there is a signifi-

TABLE II(*a*).—*Comparison of Patients by Legal Status. Number of Admissions.*

Number of admissions in 10-year follow-up.	Legal status in Period B.								All cases in Period A	
	Certified.		Voluntary.		Mixed.*		All cases.			
	No.	%.	No.	%.	No.	%.	No.	%.	No.	%.
Staying throughout	37	53·6	6	8·2	7	15·6	50	26·7	243	42·8
Only one completed admission	23	33·3	52	71·2	7	15·6	82	43·9	235	41·4
Two admissions	7	10·2	12	16·4	16	35·5	35	18·7	65	11·4
Three or more	2	2·9	3	4·2	15	33·3	20	10·7	25	4·4
Total	69	100·0	73	100·0	45	100·0	187	100·0	568	100·0

* Detained under more than one section of the Act during the period(s) of stay in hospital.

TABLE II(*b*).—*Duration of Stay of Patients who had only One Admission in 10 Years Follow-up Period.*

Duration of stay.	Legal status in Period B.								All cases in Period A.	
	Certified.		Voluntary.		Mixed.*		All cases.			
	No.	%.	No.	%.	No.	%.	No.	%.	No.	%.
Less than 5 months	7	30·4	31	59·6	2	—	40	48·8	44	18·7
5 months	9	39·2	11	21·1	3	—	23	28·0	102	43·4
10 ,,	5	21·7	7	13·5	2	—	14	17·1	69	29·4
40 months and over	2	8·7	3	5·8	—	—	5	6·1	20	8·5
Total	23	100·0	52	100·0	7	—	82	100·0	235	100·0

cant excess of patients who stay for less than 10 months in B and an excess of those who stay between 10 and 39 months in A, but no significant differences with regard to those who stay 40 or more months. (Total Chi square = 28·4; d.f. = 3; P is less than ·01: 83 per cent. of total Chi square due to excess of short stay patients in Group B). If we take only the certified patients in Group B we find no significant differences between them and Group A (Chi square is less than 7·815; d.f. = 3; P is greater than 0·05).

Table II (*c*) refers to the mean total stay in hospital during the ten years after first admission of all patients except those who died during this period. In Group B as a whole schizophrenic and affective patients have significantly shorter stays than those in the corresponding diagnostic categories in Group A. (Schizophrenics, difference = 13·6 months, S.E. difference = 5·87, P = ·02: Affectives, difference = 16·9 months, S.E. difference = 5·83, P is less than ·01) but there is no difference between the patients in the atypical category. In Group B we find without exception that certified patients have the longest stay and voluntary patients the shortest stay in each diagnostic group. The means for each diagnosis separately and for all diagnoses together of certified patients in Group B are not significantly different from those of corresponding patients in Group A. Fig. 1 summarises the data for mean total duration of stay, showing the above-mentioned distinctive features.

In Table II(*d*) the distribution of patients according to total time spent in hospital is shown by diagnosis and group. Patients in Group B with affective disorders and schizophrenia are found in larger proportions in the short stay categories than in Group A, but this difference is not seen in patients with atypical disorders. Comparison of certified schizophrenics in Group B with schizophrenics in Group A shows very little difference.

It will be seen that there are significant differences between the two groups

TABLE II(*c*).—*Mean Total Duration of Stay* (*deaths excluded*).

Diagnosis.	Legal status in Period B.				All cases in Period A.
	Certified.	Voluntary.	Mixed.*	All cases.	
Schizophrenia—					
Number of patients	54	19	25	97	330
Mean total stay (months)	84·6	49·0	61·1	71·6	85·2
Standard error	6·8	12·6	9·2	5·2	2·7
Affectives—					
Number of patients	3	41	9	53	143
Mean total stay (months)	55·0	14·6	27·3	19·0	37·9
Standard error	103·0	4·5	12·2	4·5	3·7
Atypical—					
Number of patients	13	13	11	37	95
Mean total stay (months)	62·1	21·7	49·5	44·1	44·0
Standard error	15·7	9·2	11·5	7·6	4·8
All diagnosis—					
Number of patients	69	73	45	187	568
Mean total stay (months)	79·1	24·8	51·5	51·2	66·4
Standard error	6·2	4·7	6·5	3·7	2·2

* Detained under more than one section of the Act during the period(s) of stay in hospital.

and that the outcome tends to be more favourable in Group B. However, this improvement shows a consistent linkage with legal status and would seem to be due entirely to the admission of voluntary patients in the second period, disappearing when they are excluded from consideration.

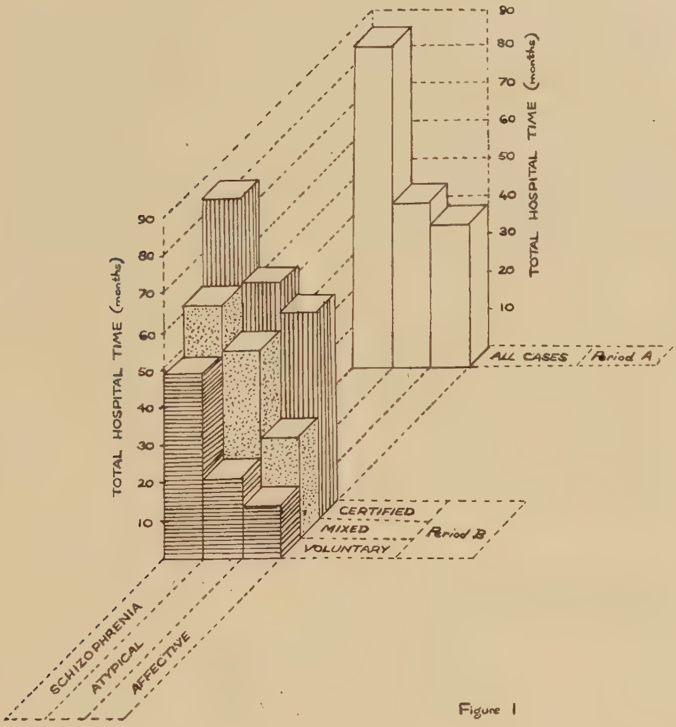

FIG. 1.

TABLE II(*d*).—*Distribution of Patients by Duration of Stay and Diagnosis in the Two Periods.*

Diagnosis and period.	Cumulative per cent. persons with total hospital time less than 10 mths.	20 mths.	40 mths.	60 mths.	80 mths.	100 mths.	120 mths.	Per cent. persons staying 120 mths. or more.
Schizophrenia—								
All in Period A	17·3	22·7	27·9	31·2	33·0	35·8	40·3	59·7
Certified in Period B	20·0	23·6	29·1	30·9	32·7	36·4	43·6	56·4
All in Period B	23·7	32·0	36·1	43·3	46·4	48·5	59·8	41·2
Affectives—								
All in Period A	43·7	58·4	69·7	73·9	73·9	80·3	81·7	18·3
All in Period B	60·4	75·5	90·6	90·6	90·6	92·5	92·5	7·5
Atypical—								
All in Period A	34·4	54·2	65·7	69·8	71·9	75·0	79·2	20·8
All in Period B	37·8	48·6	62·2	64·9	70·3	81·1	81·1	18·9

THE EFFECT OF THE NEW PHYSICAL TREATMENTS.

Of the 200 patients in Group B, 69 received some form of physical treatment for their psychiatric condition, 49 having E.C.T., 11 convulsive therapy induced by drugs, 8 insulin coma treatment alone, 4 insulin coma in addition to convulsive therapy, 1 modified insulin alone, 1 modified insulin in conjunction with E.C.T. and 1 patient receiving E.C.T. also had a leucotomy. The proportions of treated and untreated patients were similar in each diagnostic group and there were no differences between the proportions of discharges in the treated and untreated groups. Among patients with affective disorders there was a significant excess of treated cases among those with a total hospital stay of more than 12 months in hospital and correspondingly, a significant excess of untreated cases among those with a stay of less than 12 months (Table III).

TABLE III.—*Total Duration of Stay among Treated and Untreated Cases in Period B.*

	Number of cases.					
	Treated.		Not treated.			
Diagnosis and duration.	Obs.	Exp.	Obs.	Exp.	Chi square.	Probability.
Schizophrenia—						
<12 months	9	10·934	19	17·066	<5·991	$P > 0{\cdot}05$
12– ,,	6	7·419	13	11·580		
60– ,,	26	22·649	32	35·351		
Total	41		64			
Affective disorders—						
<12 months	5	9·68	30	25·320	7·89 (with Yates correction)	$P = 0{\cdot}02$
12– ,,	6	4·28	7	8·72		
60– ,,	5	2·54	2	4·46		
Total	16		39			
Atypical disorders—						
<12 months		5·95	11	11·05	<5·99	$P > 0{\cdot}05$
12– ,,	3	3·50	7	6·5		
60– ,,	5	4·55	8	8·45		
Total	14		26			

This seems to be due to the rather conservative expectant policy adopted at most of the hospitals towards these patients. In the other two diagnostic groups there were no differences with regard to total hospital stay between the patients who had and those who had not received physical treatments. Among the patients staying less than 12 months, 68 per cent. of the schizophrenics, 86 per cent. of affectives and 65 per cent. of the atypical cases received no physical treatment whatsoever. The readmission rate (57 per cent.) of treated affective cases who were discharged at least once during the follow-up period was significantly higher than that (16 per cent.) of untreated cases (Chi Square for 1 degree of freedom 8·542, P is less than ·01); there were no statistically significant differences between the rates for treated and untreated schizophrenic and atypical cases. Although one would not regard these figures as conclusive evidence against the physical treatments used, it is nevertheless clear that they cannot have played a substantial part in the production of the differences between Groups A and B.

OTHER PROGNOSTIC FACTORS.

As the history of many of the patients in Group B was known the opportunity was taken to investigate the effect of factors which it had been impossible to examine in the previous investigation.

A history of psychotic illnesses in parents or siblings was given for 52 of the patients; in 109 patients the parents and siblings were known to have been free from psychosis; in the remainder the family history was unknown. No significant differences were found regarding mean stay and frequency distribution in the different period groups between those patients who had a positive family history and those who had not.

The prognostic significance of duration of symptoms before admission was investigated; for this purpose apparent remissions were ignored and the first appearance of mental symptoms was regarded as the start of the illness. Tables IV(*a*) and (*b*) exhibit the findings. On the whole those patients with a short history tend to have a shorter stay in hospital, but the only significant difference found was between the group with a history of less than 6 months and those with one of more than 12 months (difference = 35·3 months, S.E. of difference =13·9, $P = \cdot 01$).

TABLE IV(*a*).—*Total Duration of Stay in relation to Duration of symptoms Before Admission. Patients in Period B only. (Mean Total Stay).*

Duration of symptoms.	Mean stay and standard error (months).	Median stay (months).	No. of patients.
Less than 6 months	42·5 ± 4·9	9·6	102
6 months–	49·1 ± 10·4	15·0	22
12 months–	77·8 ± 13·0	120·0	18
24 months or more	47·3 ± 9·2	10·0	28
Not recorded	85·0 ± 10·9	81·1	17

TABLE IV(*b*).—*Frequency Distribution.*

Total stay in hospital.	Duration of symptoms.					
	Less than 6 months.		6 months or more.		Not recorded.	
	No.	%.	No.	%.	No.	%.
Less than 10 months	45	44·1	21	30·9	3	17·6
10 months–	25	24·5	19	27·9	1	5·8
60 months–	13	12·7	5	7·4	5	29·5
120 months or more	19	18·6	23	33·8	8	47·1
Total	102	100·0	68	100·0	17	100·0

DISCUSSION.

The essential finding is: that in the latter period there is a higher proportion of patients with a favourable outcome and this appears to be due to the admission of a large proportion of voluntary, and presumably less seriously ill, patients in the latter period. There were only 8 temporary patients, all but 2 being included in the *changed status* category, so that these have not been considered separately. The inference to be drawn from these results is that the apparent improvement in the prognosis of patients admitted in recent years is due more to the effect of the Mental Treatment Act (1930) in admitting less severely ill patients to mental hospitals than to therapeutic advances. A possible fallacy in the interpretation of these results can be suggested: namely, that some of the patients now admitted under Voluntary Status would formerly have been admitted under certification, and if these had a particularly favourable outcome then the certified patients in period B would not be comparable with the whole group in period A. The chief reason for believing that this might be so is that there might be a tendency to certify those patients whose illness appeared long-lasting and chronic rather than to treat them as voluntary patients. However, it is noteworthy that when the three groups of patients in period B, i.e., certified, voluntary and mixed, are compared with respect to duration of illness before admission we find no significant differences. The length of history was ascertained for all but 19 of the 200 patients. Among certified patients 59 per cent., among voluntary 62 per cent. and among mixed 57 per cent. had histories of less than six months' duration; a history of duration of between 6–24 months was elicited in 28 per cent. of certified, 15 per cent. of voluntary and 26 per cent. of mixed groups, whereas in the certified group 13 per cent. had a history longer than two years and the corresponding figures for the voluntary and mixed groups were 23 per cent. and 17 per cent. respectively. We have seen earlier that length of history was probably associated with length of hospital stay, and in respect of this prognostic criterion at any rate, the certified patients in B were not more unfavourably placed than the voluntary patients at that time.

If patients are being admitted at an earlier stage of their illness and are more readily influenced by treatment one would expect as a result a fall in the long stay population of the mental hospitals, which has not taken place. In fact, in Period B 75 per cent of the patients whose total stay in hospital during the follow-up period was less than 12 months received no physical treatment whatsoever so that the preponderance of short-stay cases in Period B over those in A (see Table II(*d*)) cannot be attributed to the effects of physical treatment. There is certainly a marked tendency for those with less than six months' history to do well, but it seems likely that many of them would have recovered without inpatient treatment and that most of them would not have been admitted to mental hospitals in 1930.

The practical significance of these results lies in the fact that there is a tendency to regard the existing overcrowding in mental hospitals as a short-term effect of increased admission rates. Hopes have been expressed that the introduction of physical treatments would in time greatly reduce the chronic mental hospital population and if this were so the current overcrowding problem would be a matter of less urgency. There has been little statistical evidence to support this viewpoint (Alexander, 1945; Salzman, 1947; Rees, 1949; Norris, 1952) and the rapid turnover of mildly ill psychotic patients now being admitted to mental hospitals will not lessen the need for an increase of mental hospital accommodation.

SUMMARY.

A group of 200 patients suffering from functional psychoses who had passed through an observation ward and been admitted to a mental hospital between May 1940 and May 1942 was followed up for a period of 10 years. Their duration of stay in hospital was compared with that of a similar group first admitted to a mental hospital in 1930. In the second group the average length of stay was significantly less and there was a higher proportion of patients whose stay in hospital was short but of these only 25 per cent. received some form of physical treatment. The evidence suggests, therefore, that the differences found were due in the main to the reception of a less severely ill type of patient into the mental hospitals as a result of the Mental Treatment Act and to the increasing confidence of the public in the mental hospitals.

ACKNOWLEDGMENTS.

We are indebted for further help to all those who assisted us in the previous follow-up investigation, Miss Fisher, however, having taken the place of Mrs. Green ; also to the War Office for information regarding Service patients and to the Board of Governors of Bethlem Royal Hospital and the Maudsley Hospital for financial support from their research fund.

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MYSOLINE IN EPILEPSY: A COMPARISON WITH OLDER METHODS OF TREATMENT.

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The purpose of this paper is to report on a small series of cases treated with mysoline (5-phenyl-5-ethyl-hexahydropyrimidine-4:6-dione) and to contrast the results with those obtained with the established anticonvulsants phenobarbitone and soluble phenytoin.

The 11 patients selected for clinical trial were all subject to major epilepsy and in nine cases minor attacks were also frequent. The selected group represented cases wherein the attacks had been in some instances well and in other instances poorly controlled by these established anticonvulsants. No patient treated with mysoline by us has been excluded from this group. The ages of the patients ranged from 12 to 59. In all cases the physical health was good.

All patients in the series had received treatment with phenobarbitone only for at least one year before commencing treatment with mysoline. The transition to mysoline was achieved slowly and required 3–6 weeks according to what was considered to be the maximum safe dose for the patient. Continuous treatment with mysoline was then given for 80 days, after which time the drug was withdrawn and the series treated for a similar period on phenobarbitone and, where indicated, soluble phenytoin.

Table I.—*Dosage of Mysoline.*

Case.	Mysoline per day in grams.	Factors limiting dosage.
1	1·5	Progressive reduction of W.B.C. to 3,000/c.mm.
2	1·5	Reduction of W.B.C. to 3,000/c.mm. Toxic symptoms: ataxia, slurred speech.
3	0·75	Progressive reduction of W.B.C. to 3,000/c.mm.
4	0·75	Progressive reduction of W.B.C. to 2,000/c.mm.
10	0·75	Severe status epilepticus during transition.
11	0·75	Fatal status epilepticus during transition.
5	0·75	Drowsiness persistent
6	0·75	Slight fall in W.B.C. Age (16).
7	0·75	,, ,,
8	0·75	,, ,,
9	0·50	Age (12).

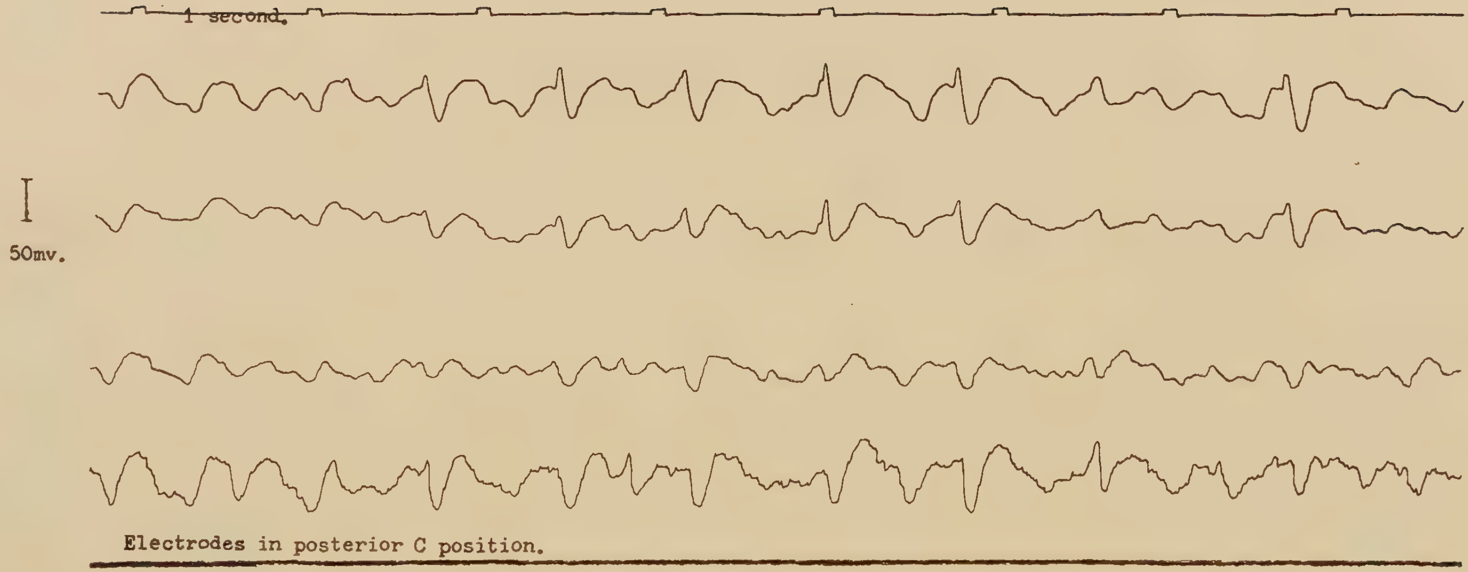
From the above table it will be noted that the estimated maximum safe dose of mysoline was lower than in previous reports, that serious complications occurred during the period of drug transition and that the majority of the patients maintained on mysoline 0·75 gm./day or more developed either overt toxic symptoms or a clinically significant fall in the white cell count.

During the drug transition to mysoline two patients developed exceptionally severe status epilepticus In the first case the patient was aged 17 and in the previous year had had 10 major and two minor fits while receiving phenobarbitone. The status supervened suddenly 12 days after the commencement of transition at a time when the patient was receiving mysoline and phenobarbitone in divided and balanced doses. After 12 hours this status was eventually controlled with difficulty using ether, parenteral paraldehyde and lumbar puncture. Treatment with mysoline was thereafter discontinued. The patient has since remained controlled by phenobarbitone. The second case developed an equally severe and prolonged status 16 days after the commencement of transition ; but, though the status was controlled in four hours, sporadic fits continued until pneumonia developed three days later and the patient, aged 20, died after a further 24 hours. In the previous year there had been good control with moderate doses of phenobarbitone and no major and only seven minor attacks had occurred during this period. This patient had, however, had a severe status two years previously as a result of which there was bilateral loss of vision of central origin which perisisted for several weeks. In both these cases transition had been slow and, as with the other patients in this series the technique of transition was carried out on the lines adopted by earlier observers.

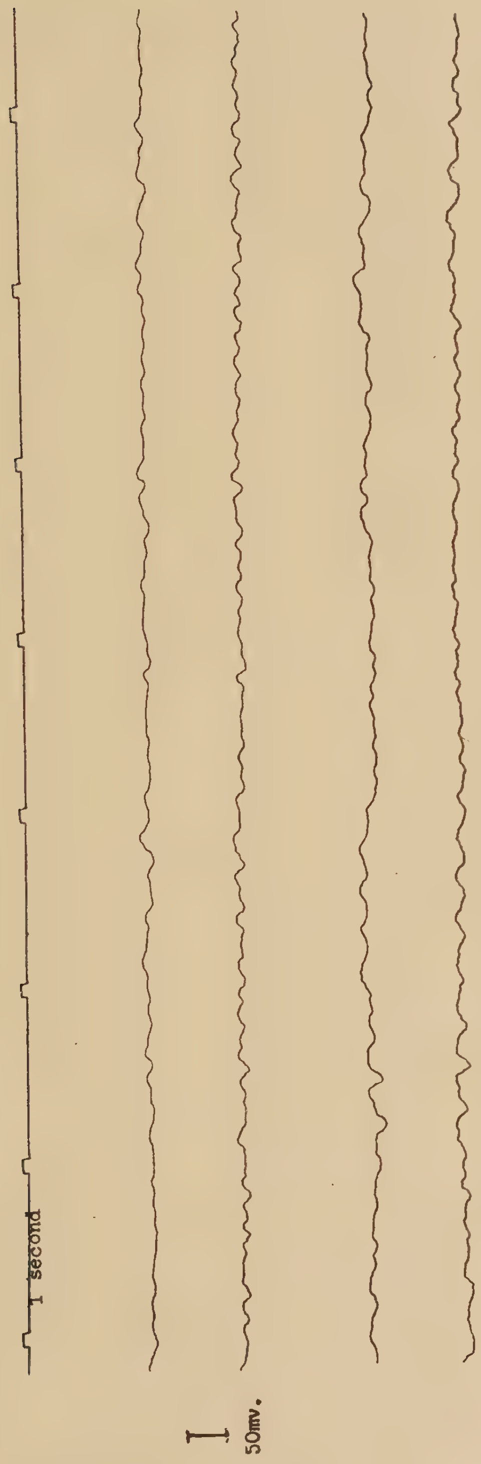
Toxic symptoms were virtually absent during the first two weeks of drug transition. After four weeks, however, one patient became persistently drowsy and for this reason the dosage of mysoline was not increased beyond the 0·75 gm. which was at that time being administered daily in divided doses. In this case some degree of drowsiness persisted throughout the remaining period of clinical trial. In a second case ataxia and slurring of speech developed after six weeks on mysoline 1·5 gm./day. These toxic symptoms were transient but returned again in the eleventh week, appearing in conjunction with a progressively falling total white cell count. On two successive days the count was confirmed to be 3,000/c.mm. and it was decided to discontinue mysoline on the grounds of toxic effects and of clinically increased epileptic activity.

In all patients receiving mysoline it was considered essential to perform a white cell count at least once per week. No significant red cell changes occurred ; but four cases out of nine showed a clinically significant fall in the total white cell count, the differential count being unaffected. Three other patients showed a moderate fall in the white count, not clinically significant.

Two patients only were maintained on mysoline 1·5 gm./day. Both developed a leucopenia of 3,000–3,200/c.mm. This degree of leucopenia was reached in one case four weeks and in the other five weeks after treatment was commenced. The counts did not improve until after the mysoline had been discontinued. Of the six patients receiving mysoline 0·75 gm./day, two developed a similar degree of leucopenia, the times being five and seven weeks after the commencement of treatment. The more slowly developing leucopenia was the more severe and three weeks later this white cell count had dropped to 2,000/c.mm. This figure was confirmed after 24 hours and mysoline treatment discontinued.

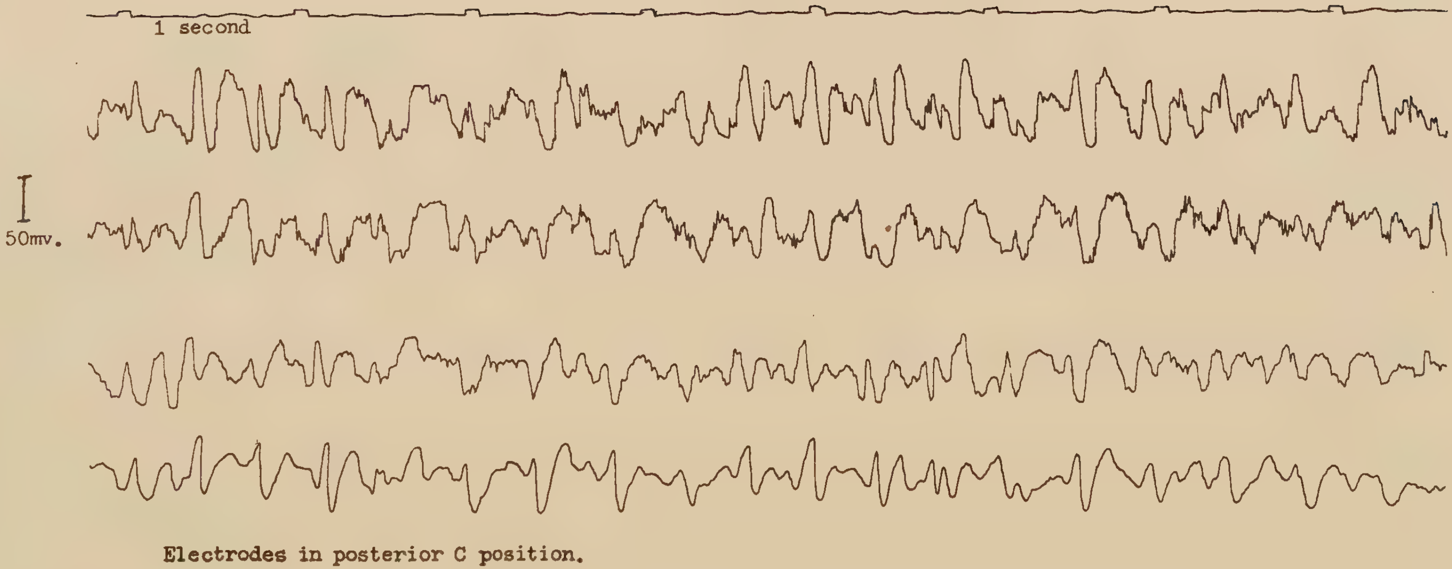

1 second.
50mv.
Electrodes in posterior C position.

CASE I.—Recording during tenth week of treatment with mysoline.



Electrodes in posterior C position

Case 1.—Recording during fourth week of subsequent treatment with soluble phenytoin.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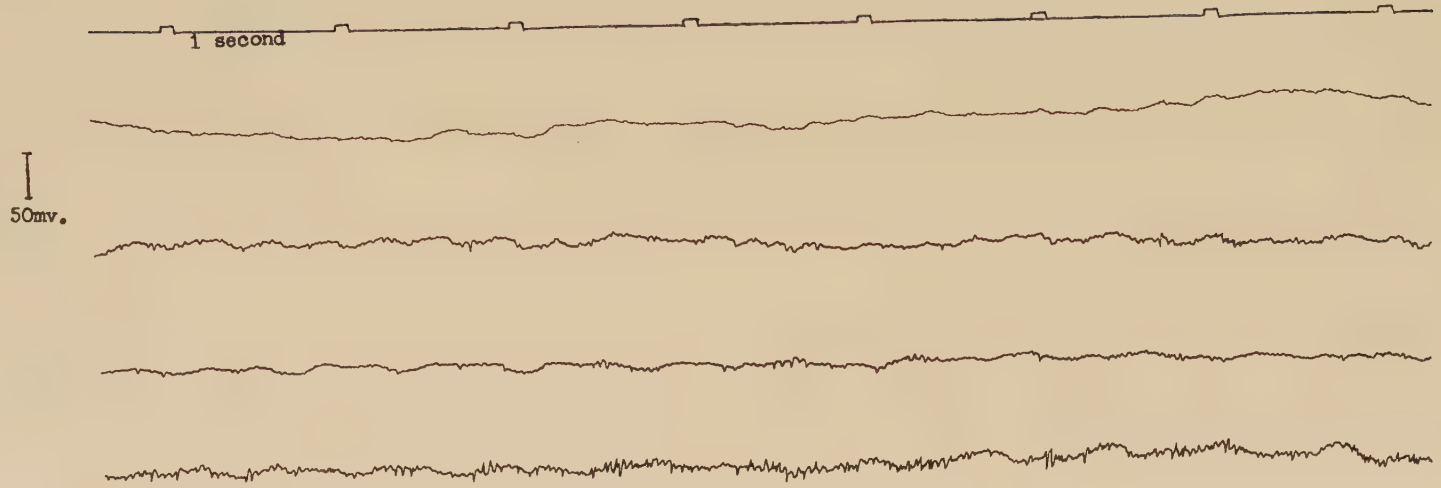
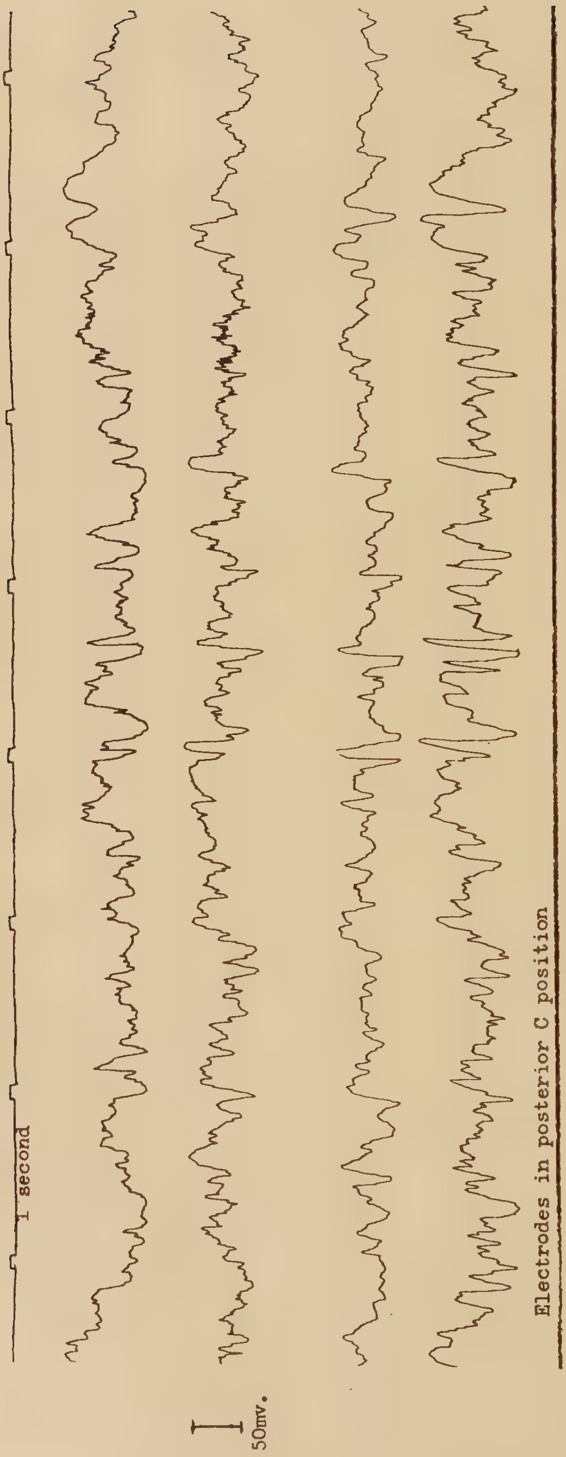
CASE 5.—Recording during tenth week of treatment with mysoline.

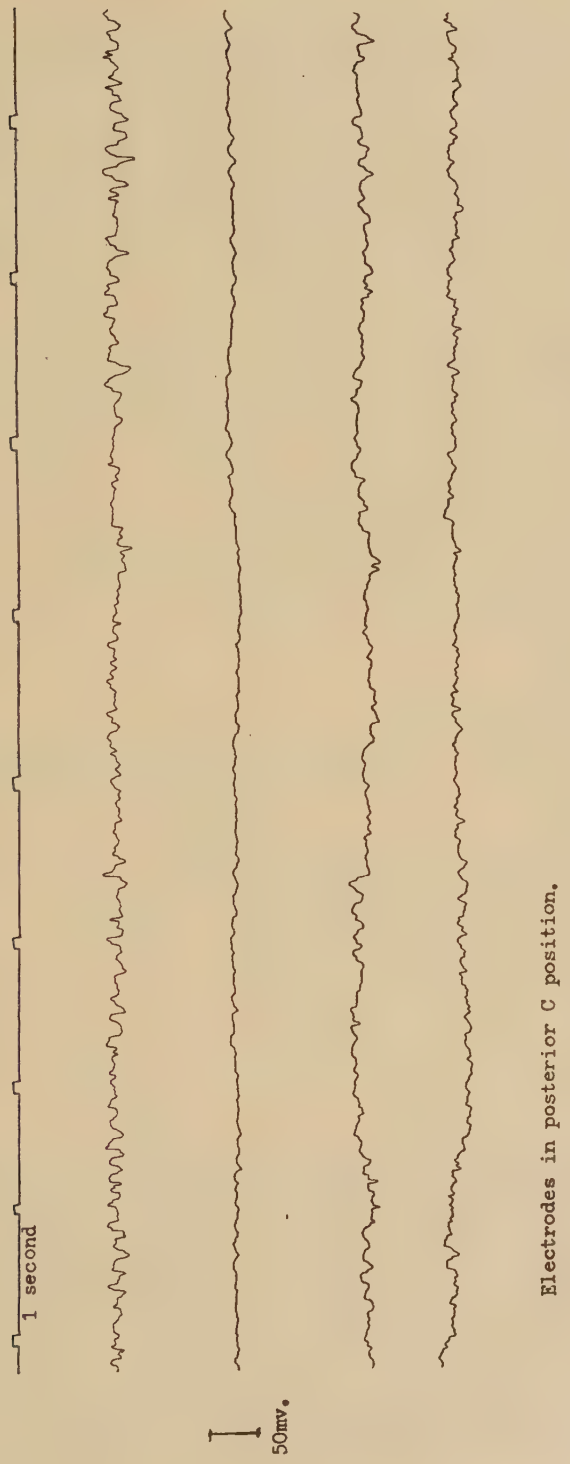


Electrodes in posterior C position.

Case 5.—Recording during fourth week of subsequent treatment with soluble phenytoin.



Case 6.—Recording during tenth week of treatment with mysoline.


1 second
50mv.
Electrodes in posterior C position.

Case 6.—Recording during fourth week of subsequent treatment with soluble phenytoin.

TABLE II.—*Total White Blood Counts during Treatment with Mysoline.*

Case.	Mysoline (gm./day).	White count before mysoline course.	Total white blood counts during mysoline treatment. 3rd week.	4th week.	5th week.	6th week.	7th week.	8th week.	9th week.	10th week.	Count one month after conclusion of mysoline treatment.
1	1·5	6,400	4,300	3,200	3,400	3,800	3,500	3,400	3,200	3,000	4,400
2	1·5	5,800	4,800	4,500	3,000	3,000	3,400	4,200	3,600	3,300	5,400
3	0·75	5,500	4,500	4,100	3,000	3,800	3,500	3,400	3,600	3,600	4,700
4	0·75	5,300	5,600	4,600	3,600	3,900	3,000	3,100	3,600	2,000	3,900
5	0·75	7,800	8,000	8,000	6,400	6,200	6,200	5,000	5,000	5,100	6,800
6	0·75	5,000	5,400	5,600	5,000	5,200	5,000	4,600	4,800	4,600	6,400
7	0·75	7,400	8,000	7,500	7,800	7,600	7,200	8,000	8,200	7,600	7,400
8	0·75	8,500	8,300	6,800	7,200	7,400	7,000	7,000	7,100	7,200	7,800
9	0·50	8,200	8,800	5,500	6,500	6,300	6,700	6,700	7,000	7,100	8,100

The blood changes in these patients were unaccompanied by other danger signs but caused anxiety and in some cases made it necessary to examine the patient and blood daily. Toxic symptoms and blood findings were indeed the chief reason why, in five cases out of the nine, the daily maintenance dose of mysoline could not safely be increased beyond the tabled figures. Even so, comparatively low maintenance doses were associated with persistent blood changes sufficiently severe to warrant discontinuation of mysoline at the end of 80 days trial. In our opinion, such blood changes should be regarded as a serious complication liable to occur in mysoline treatment to a greater extent than with the established anticonvulsants for either major or minor epilepsy.

Anticonvulsant Effects of Mysoline.

TABLE III.—*Results of Treatment of Major Epilepsy with Mysoline.*

Case.	Patient. Sex.	Age.	Mysoline per day in gm.	Incidence of major attacks. Rate/year on phenobarbitone.	Rate/year on mysoline.	Per cent. change.
1	M.	25	1·5	66	83	+26
2	M.	59	1·5	8	36	+350
3	M.	49	0·75	10	41	+310
4	M.	57	0·75	5	0	−100
5	M.	28	0·75	28	77	+175
6	M.	16	0·75	24	329	+1,260
7	F.	17	0·75	10	24	+140
8	F.	57	0·75	1	7	+600
9	F.	12	0·50	0	25	> 100

In the above assessment, a major attack was considered to have occurred if there was unconsciousness, convulsion and falling. It was noted that of this small series only one case showed any improvement. He was rendered free from fits but developed a leucopenia of 2,000/c.mm. on account of which mysoline treatment had to be abandoned. In the other eight cases there was a marked increase in the major attacks and in most cases it was an increase not only in the frequency but also in the severity and duration of the fits. Post-epileptic confusion and drowsiness were more prolonged. Behaviour was unchanged. There was no desire for further social activities or work and no subjective feeling of improved well-being. In all nine cases it was decided to discontinue mysoline.

In contrasting the effectiveness of phenobarbitone and mysoline it can be seen that six of the patients were originally well controlled with phenobarbitone having on average 5·7 major attacks per annum: during the treatment with mysoline the rate of major attacks increased in five cases and the average rose to 42 per annum. After a further transition these patients were again returned to phenobarbitone maintenance for a period of 80 days and the incidence of major fits fell to an average of 6·2 per annum. In these cases it was considered that as an anticonvulsant mysoline had proved less effective than phenobarbitone.

In the three cases poorly controlled with phenobarbitone there was with mysoline treatment a slight increase of the major attacks in one case and a marked increase in the other two. After the mysoline trial all three cases were subsequently well-controlled in the absence of toxic symptoms by soluble phenytoin alone. In these three cases the comparative clinical findings were as follows:—

	Major attacks in 80 days.		
Case.	With phenobarbitone.	With mysoline.	With soluble phenytoin.
1	15	18	0
5	6	16	5
6	5	72	6
	26	106	11

For these cases mysoline was assessed as inferior both to phenobarbitone and soluble phenytoin as a major anticonvulsant.

TABLE IV.—*Results of Treatment of Minor Epilepsy with Mysoline.*

		Minor attacks.		
Case.	Mysoline per day in gm.	Rate/year on phenobarbitone.	Rate/year on on mysoline.	Per cent. change.
2	1·5	10	0	−100
3	0·75	8	23	+188
4	0·75	15	9	−40
5	0·75	48	38	−21
6	0·75	1,057	4,628	+320
7	0·75	53	31	−41
8	0·75	9	0	−100

The above seven cases showed minor epileptic activity requiring anticonvulsant control. For clinical purposes a minor attack was considered to have occurred when there was transient loss of consciousness without convulsions. The above figures show that two patients were rendered free from minor attacks by mysoline. In one of these cases, however, there was an associated increase in the incidence of major attacks while the second case reverted to a clinical picture of major epilepsy.

Three other cases did show a 20–40 per cent. improvement whereas the remaining two showed a considerable increase in the minor attacks. This evidence is suggestive of some slight improvement in minor epilepsy following treatment with mysoline.

TABLE V.—*Summary of Results of Treatment of Major and Minor Epilepsy with Mysoline.*

	Free from attacks.	Much improved.	Improved.	Fits increased.
Major attacks	1	0	0	8
Minor attacks	2	2	1	2

Alterations in the Electroencephalograph.

An E.E.G. follow-up was carried out on all patients in this series, records being taken monthly before, during and after all courses of treatment.

TABLE VI.—*Variations in E.E.G.*

Case.	During phenobarbitone treatment (1952).	During mysoline treatment.		During subsequent treatment.	
		After 30 days.	After 80 days.	With phenobarbitone.	With soluble phenytoin.
1	++	++	++	..	N
2	N	+−	+−	N	..
3	N	N	N	N	..
4	N	+−	+−	N	..
5	++	++	++	..	N
6	++	++	++	..	+−
7	+−	N	N	N	..
8	+	+	+	+	..
9	+	+	+	+	..

Interpretation of symbols :
N = Recording within normal limits both resting and during hyperventilation.
+ − = Non-specific dysrhythmia, negative for epilepsy.
+ = Recording with characteristic epileptic forms, positive for epilepsy.
+ + = Recording strongly positive for epilepsy.

Before mysoline treatment all patients were receiving phenobarbitone and their E.E.G.s were recorded. After eighty days' treatment on mysoline, six patients were replaced on phenobarbitone and three patients on soluble phenytoin and their E.E.G.s again recorded. The three patients treated with soluble phenytoin (and whose previous records had been consistently strongly positive for epilepsy) all gave recordings negative for epilepsy and in two cases the E.E.G. became normal. Of the E.E.G.s of those receiving phenobarbitone four were normal and two remained positive for epilepsy. From the table it will be seen that the E.E.G.s after 30 days and 80 days of mysoline treatment respectively were on the whole worse than the results obtained with phenobarbitone or soluble phenytoin. In no case did a record previously or subsequently positive for epilepsy become normal or negative for epilepsy following the administration of mysoline.

Cost.—In these days when the medical profession is being constantly exhorted to economize in prescribing, it is felt that a comparison of the cost of treating patients with phenobarbitone, soluble phenytoin and mysoline (I.C.P.) should be made.

TABLE VII.—*Comparison of Treatment Costs.*

Drug.	Maintenance dose per day.	Approximate cost per patient per year.
Phenobarbitone B.P.	Tab. gr. I *t.d.s.*	II/–
Soluble phenytoin B.P.C.	Capsule gr. I½ *t.d.s.*	17/6
Mysoline (I.C.P.)	Tab. gm. 0·25 *t.d.s.*	£8

SUMMARY.

A small group of epileptics have been treated with mysoline. Major epileptic activity was increased in eight cases out of nine. One case was rendered free from fits although his E.E.G. did not improve. There was slight improvement in one-third of cases with minor epilepsy. E.E.G.s were unimproved after mysoline. Mysoline is therapeutically less effective than phenobarbitone or soluble phenytoin.

In this series two cases developed status epilepticus during orthodox drug transition. One status proved fatal. Toxic symptoms, in particular significant falls in the total white blood counts, occurred in more than half the patients and necessitated an uneconomical degree of clinical examination and pathological investigation certainly greater than that required during treatment with established anticonvulsants.

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FURTHER PSYCHOMETRIC EVALUATION OF THE EFFECT OF MEPHENESIN ON ANXIETY

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In a previous article (Ewing and Mendenhall, 1953) we reported the results of an experimental investigation devised to test the effects of mephenesin on anxiety. Rigid controls were employed, involving the use of inert tablets for comparison purposes, as well as other safeguards to eliminate subjective factors on the part of the examiners. Using the Digit Span test-retest as an index of anxiety, it was found that no statistically significant diminution of anxiety was obtained with doses of up to 2·0 gm. mephenesin orally.

In addition, using a simple questionnaire, patients described their subjective experiences with both active and inert tablets. The effects of suggestion were marked throughout.

It was concluded, from the psychometric and clinical data obtained, that mephenesin is of little value in alleviating subjective experiences of anxiety.

The Present Study.

Because we realized the dangers inherent in the possible lack of validity of the Digit Span test-retest as a measure of anxiety we decided to repeat the psychometric part of the previous experiment, substituting the Rorschach-Behn test-retest for the Digit Span test-retest as a measure of anxiety

Method.

The subjects used were male voluntary patients in the North Carolina Alcoholic Rehabilitation Centre. These men are treated purely by a régime of good diet and vitamins, community life, and daily psychotherapy ; none of them was receiving any drug apart from the test doses of mephenesin and of the inert control tablets. All the patients were sober from the time of admission, and were not admitted to the centre in acute alcoholic conditions.

As the drug was not being tested for any specific effect on alcoholism, there was no particular virtue in testing this group, except that we had here a suitable sample for the experiment. Patients in the centre are given various psychological tests and psychiatric interviews, so that the tests with mephenesin were readily accepted as being merely part of the routine.

At no time did the subjects know that tests were being conducted on mephesin, nor did the attendants who administered the tablets know the nature of the drug. Only the authors were aware of this, and not until the end of the experiment did we correlate the tables to show which patients received which tablets on which test day. When administering the tests the psychologist did not know whether active or control tablets had been given to each subject.

The tablets were known simply as " A " and " B," and which tablets were to be given first was determined from a table of random numbers, to which the chief attendent added the patient's name at the time of admission. Tablets " A " and " B " were similar in appearance.

Each patient was tested between the twenty-first and twenty-sixth day after admission. He received first one set of tablets on one test day, and the other tablets on the following test day. The Rorschach or the Behn-Rorschach (Zulliger, 1941) was given to each patient one hour after the administration of the tablets. The choice of whether the Behn or the Rorschach was to be given first was determined from a table of random numbers. The alternate form of the test was then administered on the following day, one hour after the ingestion of the other set of tablets. Both tests were done at approximately the same time of day ; small groups of 2 or 3 patients were employed daily.

The entire series of 26 patients received 2·0 gm. of mephenesin and 2·0 gm. of control tablets.

USE OF THE RORSCHACH.

In any study involving the use of the Rorschach test, the problems of the validity of the test when used as a measure of the factor to be studied, and the intrusion of the subjective factor in interpretation of the test, become of importance.

Studies of the validity of the Rorschach as a measure of anxiety, and of the diagnostic signs indicating its presence, have been made by Kates (1950) and Eichler (1951). The value of the Behn-Rorschach as an alternative form of the Rorschach has been reported by Zulliger (1941) and Singer (1952). Some doubt may easily exist as to the exact comparability of the two tests. However, it was felt by the clinical psychologist (J. H. M.) that the use of random tables would tend to eliminate any error from this source. This allowed an equal number of patients to be tested with the Behn as with the Rorschach, while under the effects of mephenesin. In addition, a check was made to see if any significant difference existed between the two tests in their ability to detect anxiety (Tables I and II).

It was decided to employ two methods of arriving at the results. Since there is still much dispute as to the comparative reliability of the " sign " approach to Rorschach interpretation as opposed to " gestalt " interpretation, it was decided to use both techniques.

The " gestalt " interpretation was employed as follows : All records were scored by the system of Klopfer and Kelly (1946) and arranged on a profile sheet (Klopfer and Davidson, 1942). The records were then arranged by an assistant who knew nothing of the Rorschach, without any identification as to day of administration or tablets given. Each patient's two records were placed side by side in front of the psychologist, who then proceeded to rate the records as to "more anxiety" or "less anxiety." All of the content of the record as well as the profile and scoring totals and percentages were employed in this rating. The results are shown in Table I.

TABLE I.—"*Gestalt*" *Interpretation of Anxiety as Shown by Rorschach and Behn-Rorschach Tests on 26 Subjects Receiving Mephenesin and Inert Control Tablets on Alternate Days.*

	Number rated "more anxious."	Number rated "less anxious."	Level of significance.
Mephenesin 2·0 gm. orally	16	10	Less than 5%
Inert Tablets 2·0 gm. orally	10	16	
1st day	12	14	Less than 5%
2nd day	14	12	
Rorschach	15	11	Less than 5%
Behn	11	15	

(In both Tables I and II the level of significance was determined by chi-square, using the formula :

$$\chi^2 = \frac{2(f_o - f_e)^2}{f_e}$$

with a correction for continuity, following Goulden (1939) and Snedecor (1940).)

Following this, the profiles were rearranged, and, again without any identifying marks known to the psychologist were interpreted by him according to a seven point scale. The records were again rated as "more anxious" or "less anxious."

The seven points used were those suggested by Eichler (1951), modified in the case of the "ShW" score to fit the Klopfer and Kelley scoring. The points were as follows :

1. "W" = Number of whole responses reduced by the presence of anxiety.
2. "R" = Total number of responses reduced by the presence of anxiety.
3. "Do" = Number of oligophrenic details increased by the presence of anxiety.
4. "ShW" = Total number of disphoric shading responses increased by the presence of anxiety. In this case, Hertz's (1948) score was taken most nearly to coincide with :

   $ShW = K + KF + cF + c + \Sigma C'$ (black only).
5. "Rej." = The number of cards rejected without response will increase with the presence of anxiety.
6. "P" = The number of popular responses will decrease with the presence of anxiety.
7. "ΣC" = The weighted total of bright colour responses will decrease with the presence of anxiety.

In this article, Eichler gave evidence of the validity of the first four signs, and suggested the validity of the last three. The last three were included in this study, since the work of Kates (1950) supports their validity.

The results of the interpretation, using these seven points, are shown in Table II.

TABLE II.—*" Sign " Interpretation of Anxiety as Shown by Rorschach and Behn-Rorschach Tests on 26 Subjects Receiving Mephenesin and Inert Control Tablets on Alternate Days.*

	Number rated " more anxious."	Number rated " less anxious."	Level of significance.
Mephenesin 2·0 gm. orally	16	10	Less than 5%
Inert Tablets 2·0 gm. orally	10	16	
1st day	6	20	Less than 1%
2nd day	20	6	
Rorschach	15	11	Less than 5%
Behn	11	15	

RESULTS.

It will be readily seen from Tables I and II that no significant difference was found in the amount of anxiety shown in the tests of patients after receiving mephenesin and inert tablets. It will further be seen that no significant difference was shown to exist between the Behn-Rorschach and Rorschach in their sensitivity to anxiety.

In the case of the " sign " interpretation, a somewhat significant difference was found to exist between the first day and the second day in amount of anxiety present. We are inclined to attribute this variation to chance, since it does not reach the 1 per cent. level of significance.

It seems likely, from the above, that mephenesin is of little real value in alleviating experiences of anxiety, as measured by the Behn-Rorschach test-retest. The results of our previous experiment are thus supported. This would tend to validate the use of the Digit Span test-retest (as used in our previous study) as a measure of anxiety.

SUMMARY.

1. An experiment was devised to test the effects of mephenesin on anxiety on 26 alcoholic patients. This was as a follow-up to test the validity of a previous experiment by the authors (in which it was concluded that mephenesin is of little value in alleviating subjective experiences of anxiety).

2. Rigid controls were employed, involving the use of inert tablets for comparison purposes, as well as other safeguards to eliminate subjective factors on the part of the examiner.

3. Using the Behn-Rorschach test-retest as an index of anxiety, it was found that no statistically significant diminution of anxiety was obtained with doses of 2·0 gm. mephenesin orally.

4. It is concluded, from the psychometric data obtained, that mephenesin is of little value in alleviating states of anxiety as measured by the Rorschach

and Behn tests. The authors' results in their earlier experiment are corroborated.

ACKNOWLEDGMENTS.

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E. R. Squibb & Sons kindly supplied us with control tablets to match their product " Tolserol."

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Part II.—Reviews.

Experimental Hypnosis. Edited by LESLIE M. LECRON. New York: The Macmillan Company. Pp 476. Price 45*s*.

Serious research into hypnosis has been long delayed by the popular fear and prejudice surrounding the subject. Hypnosis can be neither defined nor explained, but hypnotic phenomena can be described, investigated and applied. The twenty papers in this book, contributed by various authors, record work done along these lines. It is impossible, in a short review, to do justice to each paper, so a summary of the contents must suffice.

A paper on the history of hypnosis is followed by three papers which describe in detail various induction techniques and the characteristics or the different levels of trance state. The dynamics of hypnosis, with special reference to resistance are discussed. An investigation into the dynamics of a hypnotist might be very valuable.

The next paper considers the hypnotic trance in relation to the state induced with barbiturates for narco-analysis, and discusses the use of drugs in the induction of hypnosis proper.

A group of papers records controlled experimental work. Hypnotic susceptibility as a function of waking suggestibility has been investigated, and so have the phenomena of " age regression " and " time distortion " under hypnosis. Interesting is the series of Rorschach tests administered at different age regressions. Two papers are concerned with the influence of hypnotic suggestion upon certain involuntary somatic functions.

Two papers describe the use of hypnosis in dentistry. The advantages to both dentist and patient appear considerable. The patient is not only analgesic, but can enjoy an hallucinated repeat of his favourite film show.

Next comes a paper on hypnosis in obstetrics. The advantages to the mother are well illustrated, both in preparation for labour and during labour.

A paper on hypnosis and extra sensory perception has important philosophical implications.

The possibility of the anti-social abuse of hypnosis has been subjected to experiment. All in all, the chief danger appears to be to the hypnotist.

The paper on the investigation of multiple personality whets the appetite, and the same may be said of the account of automatic writing. These two papers, which bear on hypno-analysis, are followed by an account of " projection techniques." The final paper shows a phobic reaction treated by hypnoanalysis. Each paper is introduced by the editor, and is followed by a comprehensive bibliography. Much of the book could be enjoyed by the lay man.

The material in this book, intrinsically fascinating, is presented objectively and discussed critically. No-one suggests that the last word on hypnosis has yet been written, but I do not think that any worker in hypnosis will wish to quarrel seriously with anything in this volume. Hypnosis has much to offer, to medicine, to psychiatry and to philosophy. This book deserves the attention of every thoughtful person. It should do much to dispel the prejudices which have hitherto surrounded this subject and stimulate the wide but co-ordinated research which is so long overdue. D. E. R. KELSEY.

If A Man Be Mad. By HAROLD MAINE. Victor Gollancz, Ltd. Pp. 435. Price 15*s*.

This autobiography of an alcoholic makes an exceptional novel, of considerable social and psychiatric value.

To a lonely, frightened child security first comes with the present of a gun. Aged 11, the child discovers the same security in a medicinal dose of brandy. This experience is often confirmed, on joining the army at 16. Imperceptibly, alcohol becomes indispensable to the child remaining within the man.

The bulk of the book relates the author's experiences at many hands in many institutions, in his struggles against his addiction. He finds horror, comedy, tragedy and—sometimes—understanding. He gains rare insight into the minds of some psychotics, which his gifts as an author enable us to share.

Recovery comes through his work on behalf of other patients.

The story, as a whole, is a grim one; but it is well written, reads easily, and deserves to be read. D. E. R. KELSEY.

The Case Against Psycho-Analysis. By ANDREW SALTER. Medical Publications, Ltd. Pp. 158. Price 10*s*. 6*d*.

"*Sex underlies everything*: Mr. Jones wrote a story for his high school magazine only because he was sexually frustrated. Now Mr. Jones collects postage stamps and is trying to build up his savings account only because he had poor toilet training as a child." Thus Mr. Salter enunciates and illustrates one of the fundamental principles which, he asserts, guide the psychoanalyst in the treatment of EVERY man who comes into his office. This extract is typical of the tenor of the book.

Every analyst is familiar with Mr. Salter's line of argument and, aware of its possible unconscious motivation, has a certain sympathy for its author. Others may be less charitable, and will certainly doubt whether Freud was merely the muddle headed purveyor of pornography Mr. Salter implies.

D. E. R. KELSEY.

Mind and Life. By SIR ARTHUR TANSLEY. George Allen and Unwin, Ltd. Pp. 170. Price 15*s*. net.

It is rare these days to find an unprejudiced exposition of a school of thought upon any of the fundamental problems; and one can become confused by the outpourings of vigorous pens and voices, each extolling its own point of view, while doing less than justice to the views of others.

Here, in twelve essays, with great fairness and the simplicity which is possible only for the very clear thinker, the author examines the essence of current thought upon man's place in "The Divine Scheme," and the forces which cause him to function as he does.

The author uses his personal philosophy, which is based upon a firm belief in the ultimate reality of spiritual values, only to show the common factors behind the polymorphous thoughts and behaviour of men.

This book will prove of value to all of an academic, political, ecclesiastical or philosophical turn of mind. D. E. R. KELSEY.

First Contributions to Psycho-analysis. By SANDOR FERENCZI, M.D. Authorized transaltion by ERNEST JONES, M.D. The Hogarth Press and The Institute of Psycho-analysis. Price 30*s*. net.

This book includes several of the papers that now belong to the classics of psycho-analysis, such as Introjection and Transference; On Obscene Words; On Onanism; Stages in the Development of the Sense of Reality; The Ontogenesis of the interest in Money. In addition it contains Ferenczi's pioneer papers on Impotence, Homosexuality, Paranoia, Symbolism, etc.

One cannot criticize work of this class. One can only marvel at the penetrating insight of the author. And the style, as it is rendered by the translator, is a model of clarity and simplicity.

No practising analyst can afford to neglect to read these papers; nor, I would add, can anyone who essays to criticize the principles of psycho-analysis.

This book has been out of print for many years, and its reappearance is an event of considerable importance. D. E. R. KELSEY.

Psychosomatic Medicine. By FRANZ ALEXANDER. London: George Allen & Unwin, Ltd., 1952. Pp. 300. Price 21*s.*

This book is in two parts. In the first the general principles of psychosomatic medicine are given. " Psychological processes . . . are at the same time physiological processes and differ from other body processes only in that they are perceived subjectively . . . they can therefore be studied by psychological methods." " The main contribution of psychoanalysis to medicine has been to add to the optical microscope a psychological microscope . . . " " Theoretically every disease is psychosomatic . . . "

It is asserted " A mysterious and vague correlation between personality and disease does not exist . . . " but that much work has been done to elucidate the specific emotional factors in different somatic diseases, which is described in Part Two of the book.

Dr. Alexander differentiates two types of response to an anxiety producing situation, (1) preparation to deal with it actively, by an increased response of the sympathetic nervous system, found in essential hypertension and migraine, (2) retreat to " increased dependence like the small child who turns to the mother for help . . . ", thus increasing parasympathetic excitation. This regressive tendency is found to underlie many diseases, such as disturbances of the gastro-intestinal tract, thyrotoxicosis, diabetes; and, most thoroughly of all, asthma, in which there is a fantasy of regression to the womb.

These theories are given to explain a large assortment of facts found by psychoanalysis and given in the text of this book, and much of the interest and fascination of the book lies here. Thus in the history of hyperthyroid patients " a unique and striking feature is the frequency of dreams of death, caskets, ghosts, and dead persons which these patients report spontaneously."

Such facts can be confirmed by any skilled person who takes the trouble to investigate and Dr. Alexander is duly modest in respect of his conclusions— " I wish to emphasize that at the present state of our studies we are not yet able to evaluate the aetiological significance of all of these findings."

But, considering the long period of time in which the field of psychosomatic medicine has lain fallow, Dr. Alexander and his colleagues in the Chicago Institute for Psychoanalysis can be proud of what they have achieved. It is the results of their seventeen years' collaboration, which are set forth in this excellent book. C. E. H. TURNER.

Some Common Psychosomatic Manifestations. By J. BARRIE MURRAY. Second Edition. Oxford Medical Publications, 1951. Pp. 285. Price 17*s.* 6*d.*

The author accepts that there are physical manifestations of emotion. Thus he describes the physical symptom of sighing as being the response to an accumulation of carbon dioxide in the circulation, which occurs when the patient is absent minded. " It is as though the respiratory centre, so easily influenced by the emotions, indulges in day-dreaming at the same time as the patient . . . ."

But the book does not follow this psychosomatic approach beyond the functional sphere into the sphere of organic lesions; rather is it concerned with assessing " symptoms which are psychogenic and not organic."

One third of the book is devoted to miners' nystagmus because " this condition differs little from the common psychoneuroses." " Miners' nystagmus appears to have no morbid anatomy or morbid histology, and this fact, taken with its baffling lack of explanation, raises the question of an explanation on psychiatric grounds." Similarly one quarter of the book is devoted to the psychoneurotic nature of the effort syndrome.

One wonders whether the title of the book should not have been, " Some Common *Pseudo*somatic Manifestations."

The book includes much statistical matter, but reads easily.

C. E. H. TURNER.

My Son's Story. By JOHN P. FRANK. London: Sidgwick & Jackson, 1952. Pp. 174. Price 10s. 6*d*.

Psychiatrists and the parents of mentally defective offspring are fortunate that this little book has been written. It is opportune that it should be published at a time when the National Health Service is striving to improve the institutional accommodation for mental defectives.

Mr. Frank, a teacher of law at an American university, writes of the reactions of his wife and himself to discovering that their first child was backward. His wife has written two of the chapters—" if our experience can help anyone else, then I suppose it is worth while opening our personal lives like this."

It was difficult to accept that the baby was defective, " somehow we still had the conviction that no ultimate disaster *could* befall us."

But with sense and sensibility the parents reoriented themselves—" we have learned to hope for less and less, and always to hope with the original intensity of the first hope."

Institutionalization was decided upon in spite of many initial misgivings of what might result—" he may have no affection, no opportunity to grow within the limits of his stunted capacity." The authors were able to place him in an institution, whose atmosphere quite allayed their fears.

The parents decided that they would " live with candour about their child, not to hide the fact that he existed or was defective, for that, they say, would be to develop a sense of shame and guilt.

The mother admits, none the less, that " the feelings of guilt attendant upon committing a child to the permanent care of others are more overwhelming and devastating than could possibly be described or even hinted to those who have never experienced them." The father agrees—" we were each extremely unhappy "—and this in spite of a settled conviction they were doing the right thing.

Finally they achieved peace of mind—" This doesn't mean forgetfulness, which we neither have nor want. It means lack of minute to minute concern."

The book has an introduction by Dr. Noel Burke of Cell Barnes Hospital, St. Albans.

C. E. H. TURNER.

Bedlam on the Jacobean Stage. By ROBERT RENTOUL REED, jun. Cambridge, Mass.: Harvard Univ. Press, 1952. Pp. 160. Price $3.50.

The author briefly considers Bethlem Hospital and its background from its foundation as a priory in 1247 and acknowledges his indebtedness to the writings of Dr. Hack Tuke and the Rev. E. G. O'Donoghue. Insanity as a theatrical device is then discussed and the fact stressed that the mental pathology of the Elizabethan Age became essentially functional to the plot of the drama as a medium of spectacle, and as a symbolic expression of human disillusionment. The major difference between Elizabethan and Jacobean dramatic studies of madness is said to rest in the fact that in the latter not only shock but humoral theories are essential factors in the study . The book will interest the historically-minded psychiatrist.

NORWOOD EAST.

One Little Boy. By Dorothy M. Baruch, with the collaboration of Dr. Hyman Miller. London: Victor Gollancz, Ltd., 1953. Pp. 242. Price 13s. 6*d*.

An account by a clinical psychologist of the analytical treatment of a seven year old boy who suffered from asthma and was failing at school. The treatment sessions were continued for two and a half years. As the child's aggressiveness appeared, first towards the therapist and later towards the parents, the distorted fantasies and fears associated with his sexual drives emerged. The fact that his maladjusted parents attended group therapy sessions at the same time was important. The boy won through and at the age of twelve was happy and doing well in a Junior High School. The book emphasizes the fact that parents should feel that assistance from a clinic or therapist is a friendly process and not a terrifying ordeal.

Norwood East.

Saving Children from Delinquency. By D. H. Stott, Ph.D. London: University Press, Ltd. 1952. Pp. 258. Price 12s. 6*d*.

The object of the present book by the author of *Delinquency and Human Nature* is to outline some of the preventative methods which seem to him to hold out a reasonable prospect of success. He has carefully studied his material with an obvious desire to present his conclusions impartially, and this will appeal to his readers. But some are likely to protest when the author steps out of his own sphere, and naïvely discusses the etiology of moral defectiveness, or attempts to create new mental disorders. The ordinary reader may be perplexed, the opponents of psychology and psychiatry encouraged, and psychiatrists who are concerned with offenders, and are aware of the distrust which is often associated with medical evidence, will realize the disservice to psychiatry which is likely to arise from the fanciful diagnoses—" status-neurotics," " achievement-neurosis " and " play daft neurosis "—made by the author.

Norwood East.

Primer on Alcoholism. By Marty Mann. Forword by Professor T. Ferguson Rodger. London. Victor Gollancz, Ltd. 1952. Pp. 160. Price 8s. 6*d*.

The blurb states that Mrs. Mann suffered for years from this condition and neither she or her family or friends knew what to do about it. The book provides the alcoholist and the non-alcoholic world in which he lives with information regarding the causes, the early, middle and late symptoms of the condition, and forms of treatment including alcoholics anonymous. Mrs. Mann writes primarily for Americans. But in 1951 the number of persons found guilty of drunkenness, simple and aggravated, in the courts of England and Wales was 51,239, excluding persons found guilty of driving or being in charge of a motor vehicle while under the influence of drink or drug, and the book can be recommended to those in this country who may be concerned in this complex social problem.

Norwood East.

Broadmoor: A History of Criminal Lunacy and its Problems. By Ralph Partridge. London: Chatton & Windus, 1953. Pp. 272. Price 21s.

With the approval of the authorities and the co-operation of Dr. J. S. Hopwood, C.B.E., formerly superintendent of Broadmoor, Mr. Partridge discusses legal and medical insanity before relating the history of this establishment from 1863 to 1952. Much of his account is inevitably associated with period problems and the personalities of individual superintendents, and interesting details are given of their work and times. The administration of Broadmoor is recorded with realism and without sensationalism. The overall principles of recreation and treatment are discussed. This part of the book is of special interest when compared with the administration of other mental hospitals. Psychiatrists will find the introductory chapters on legal and medical insanity particularly appropriate at the present time in view of the evidence given before the Royal Commission on Capital Punishment.

With reference to the account given of the shooting at Queen Victoria at Windsor Railway Station on 2 March, 1882, it should be noted that Mr. Partridge, like some other authors, repeats the statement that the Queen objected to the prisoner being found "*Not Guilty* on the ground of insanity" *as she saw* him fire the pistol herself. But an extract from the Court Circular issued from Windsor Castle on 3 March, 1882, and published in the *Daily Telegraph* on 4 March 1882, states: "The Queen *heard the report* (of the pistol) *but did not see* the occurrence, though Princess Beatrice, who was sitting on that side of the carriage, perceived the man raise his hand and fire." This caveat is not without interest for as the result of the Queen's reaction to the above verdict the Trial of Lunatics Act, 1883, followed and the words "*Guilty* of the act or omission . . ." were introduced in the verdict.

NORWOOD EAST.

Social Science and Mental Health. An Essay on Psychiatric Social Workers. By MARGARET ASHDOWN and S. CLEMENT BROWN. London: Routledge & Kegan Paul, Ltd. 1953. Pp. 254. Price 16s.

This book deals with a branch of social service little more than twenty years old, and will impress the reader with the authors' intimate knowledge of their subject. Sound judgement, a practical approach and occasional criticisms are presented with carefully chosen words. A close acquaintance and understanding of the tensions which confront the psychiatric social worker, who is essentially concerned with mental illness, maladjusted personalities and personal relations, are apparent throughout the book. The definition of this speciality by the American Association of Psychiatric Workers is quoted—"Social work undertaken in direct and responsible working with psychiatry"—and its merits are acknowledged. But it is pointed out that it does not suggest the element of reciprocity between social work and psychiatry and the need of each for what the other can contribute.

The authors discuss the origin and growth of psychiatric service. This is followed by examples of case work, and the selection and training of those who choose this form of work are subsequently discussed. The careers of some trained psychiatric social workers are then presented factually and impartially, and their services in clinics, hospitals and wider fields are examined. Other chapters on personal difficulties, ends and means, and on considerations of wider significance are included. Each chapter is a valuable contribution to an important book. Miss Ashdown and Miss Brown are to be congratulated.

NORWOOD EAST.

Reason and Unreason in Psychological Medicine. By E. B. STRAUSS. Foreward by SIR RUSSELL BRAIN. London: H. K. Lewis & Co., Ltd., Pp. 55. Price not stated.

Dr. Strauss has collected under the above title his Presidential Address to the Medical Section of the British Psychological Society in 1946 and his Croonian Lectures in 1952. In the preface he states he has tried to follow the middle way and in his Presidential Address he seems to point to the white line when he states, "Any and every psychological formulation is little better than a parable, or simile, or metaphor. The same is true to a certain extent of all scientific formulations . . ." He believes that psychoanalytical theory in its present form will have nothing new to offer suffering humanity, and he discusses fact and fiction in Freudian psychology with his usual insight and balanced judgment. Discussing the acceptance of formal theological systems the author pungently states: "A successful Freudian analysis results only in a person *making* good in the American sense, the idea of his *being* or *becoming* good or even *doing* good does not come into the picture."

In the Croonian Lectures Dr. Strauss considers the concept of causality and reminds us that as medical students we tended to accept the cause-effect relationship in disease. He avoids the temptation to throw light on the body-mind relationship in its causal setting, and whilst he accepts the view that the whole of medicine, including psychological medicine, is psychosomatic he finds no answer to the question itself seeing that it "has no meaning outside a twisted semantic framework." Further, he believes no causal schemata are accurate which disregard the possible operation of free choice. The value of orthodox psychoanalysis is discussed and concepts such as the Oedipus complex, infantile sexuality and the like are supported. But Dr. Strauss believes that the use to which they are put by practising analysts is often unfortunate, and points out that rigid psycho-analytical theory violates the principle of multiple aetiology; and perhaps the reviewer may add in the words of John Stuart Mill "the intermixture of effects."

These scholarly, clear and concise addresses are presented admirably. They can be re-read with pleasure and satisfaction. Psychiatrists will be grateful to the author for bringing them together under the same cover.

NORWOOD EAST.

The Tools of Social Science. By JOHN MADGE. London; Longmans, Green & Co. 1953. Pp. 294. Price 25*s.*

The generous and fully documented pages of this volume deal with the chief techniques which social scientists have introduced to advance our knowledge of an increasingly important subject. The introduction is followed by a discussion on the relevant aspects of language and logic, and the author concludes that the social scientist must be constantly on guard lest inferences based on observational material evade his logical defences and present themselves as equivalent proofs. The use of documents in social science and problems of authenticity are then examined, and it is pointed out that much social evidence is still obtained second-hand from documentary sources and that the use of documents being remote from the objects of the social scientists study tempts him to stretch his material to suit his thesis. Observational methods and their practical application receive attention, and the author states that most successful scientific discoveries are due to the fact that some observers see simultaneously more things and unsuspected things than their colleagues. Different types of interview occupy a third of the book and include subjects which can be suitably explored by the use of mass interviews, sampling and other techniques. Matter relating to the reduction of bias and the scope of experiment in social science is examined later. A final chapter on the limits of social science emphasizes the lesson of the book—that there can often be an orderly progress through the search of documents, through observations and various forms of questioning before we are prepared to experiment.

The book demands and deserves the reader's close attention. It should be read by the serious student of social science. As technical terms are avoided as far as possible contributors to the pseudo-scientific literature which inundates us to-day should profit by the author's erudite study and sound advice.

NORWOOD EAST.

A General Selection from the Works of Sigmund Freud. Edited by JOHN RICKMAN. Reprinted 1953. London: The Hogarth Press, Ltd., and The Institute of Psychoanalysis. Pp. 329. Price 10*s.* 6*d.*

Civilisation, War and Death—Selections from Five Works of Sigmund Freud. Edited by John Rickman. New and Enlarged Edition, 1953. London : The Hogarth Press, Ltd., and The Institute of Psychoanalysis. Pp. 115. Price 8*s.* 6*d.*

The first of these two volumes consists of extracts from the technical writings of Freud ; the five essays epitomized in the other volume were written for laymen. The extracts are from already published translations ; and great credit is due to Dr. Rickman for the editing which has been done extraordinarily well.

These epitomes bring the work of Sigmund Freud to a larger public, which recognizes his genius, but which is not disposed to read the full text of his writings.

Even in epitomes one still, of course, has to accept Freud's longwinded and somewhat tantalizing style, in which he may withold as long as possible the information he is about to give. Thus he fills half a page in this manner, " One method I have not yet mentioned at all . . . How would it be possible to forget . . . It is conspicuous for . . . Needless to say, it, too,. . . but it . . . on the contrary . . . Nor is it . ... rather it . . . Perhaps it . . . ," and finally the pill is given, " I am speaking, of course, of that way of life which makes love the centre of all things and anticipates all happiness from loving and being loved."

At other times Freud will unexpectedly make a good point suddenly, almost as an aside. Thus when comparing genital love and its modification in non-genital love he says " aim-inhibited love leads to " friendships," which are valuable culturally because they do not entail many of the limitations of genital love, for instance, its exclusiveness."

Everyone, of course, knows what Freud wrote about. He was quite unwilling to let many matters, important to the human race, remain covered up, laughed at and ignored. On the other hand, he even " attacked the more difficult problems " by psychoanalytic research, quite determined to put upon a scientific basis whatever knowledge he could establish.

Freud appreciated the difficulties of his task and often made comments such as these : " So little is known about the psychology of processes of feeling that the tentative remarks I am about to make on the subject may claim a very lenient judgment." And on another topic, " I cannot promise that this attempt will prove satisfactory ; it is much more in the nature of a first sounding and hardly goes beyond that." Again " I am putting forward nothing but a supposition ; I have no proof to offer." And, " Psycho-analytic research could not produce a complete and finished body of doctrine . . . "

He describes his basis of thought as follows, " Our starting point will again be the one situation which we believe we understand." But starting-points are not easy to agree upon. One fundamental axiom which Freud appears to have taken is that it is natural for men to be " savage beasts to whom the thought of sparing their own kind is alien . . . ." Freud speaks of " this primary hostility of men towards one another," and from this axiom Freud makes his close argument. Freud admits that his conclusions offer no consolation to the human race. It would seem, however, equally open for the argument to have been developed from the axiom that the " hostility of men towards one another " is a pathological situation in the human race, the cause of which has to be found.

However, Freud took his own axioms and he was quite entitled to say, " One may surely give oneself up to a line of thought, and follow it up as far as it leads . . . " Characteristically he will say " we have been driven to the hypothesis . . ." and there he was to leave it. As he truly and sensibly says, " We are forced to break off every investigation at some point until such time as the results of another attempt elsewhere can come to its aid."

Meanwhile, he is even prepared to accept a humorous criticism of one of his hypotheses. Thus he records, " To be sure, this is only a hypothesis, like so many others with which archaeologists endeavour to lighten the darkness of prehistoric times—a ' Just so Story,' as it was amusingly called by a not unkind critic (Kroeber) . . . "

One must not, therefore, be unduly upset by some of the extravagances of Freud's style or conclusions. We have his tendency to say that something is due to a certain factor " and nothing else " : thus conscience " in its origin is ' dread of the community ' and nothing else." Perhaps Freud is really only asserting, unconsciously, that that is the only way he, for the moment is regarding conscience. But Freud is, in any case, very weak in his statement of " the higher, moral, spiritual side of human nature," in spite of his somewhat pathetic defence that he is not when he says proudly " and here we have that higher nature, in this ego-ideal or super-ego, the representative of our relation to our parents." Well, that is not saying enough about "the higher, moral, spiritual side of human nature," and especially is it poor when we remember that Freud speaks of " a primary hostility " in the relationship of " men towards one another."

Nor is Freud's statement of the origin of love very satisfying or complete. " Love originates in the capacity of the ego to satisfy some of its instincts auto-erotically . . . " But we must allow him his " line of thought," there is something to be found in it if one follows his argument ; he has taken it " as far as it leads." Elsewhere " another attempt " will come to its aid and Freud is saying " love alone . . . brings a change from egoism to altruism." This " love " apparently is not originating in auto-erotism ; we must not be surprised, for truth has many facets.

Further, one must accept that the conclusions of Freud are not just arm-chair theorizing but are theories based on some startling findings in very many years of " intensive work." Thus he discovers " the conflict of opposing mental forces " ; " regression to earlier phases " ; criminality arises from a sense of guilt which is " present prior to the transgression " ; and he notes of sexual tendencies that " if they become too strong they disintegrate every group formation," but " homosexual love is far more compatible with group ties . . . —a remarkable fact, the explanation of which might carry us far."

Freud writes in one place, " Never before in any of my previous writings have I had the feeling so strongly as I have now that what I am describing is common knowledge . . . " The credit due to him even in such a case, is that he did put pen to paper and describe what others, though they knew it, had not the ability, inclination or drive to formulate, and argue from, the knowledge as they saw it. Freud had the faith to make his gigantic effort in attempting the scientific evaluation of so many problems of the mind ; and it is for this that history will remember him and that these new editions of epitomes of his works are to be welcomed.

Finally, it must be said that the technical volume of these two epitomes has a valuable index and glossary. C. E. H. TURNER.

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Dormison, A New Type of Hypnotic. Its Therapeutic Use in Psychiatric Patients.

Dormison is a drug of a new type that, when used as a hypnotic, is highly efficient and relatively nontoxic and noncumulative. It is the hypnotic of choice in elderly, senile, and arteriosclerotic patients and it has definite advantages over other hypnotics in other types of patients.

The hypnotic effect is highly specific, and dormison is of little value as a sedative since toxic or near-toxic doses are required to produce an adequate sedative effect in disturbed patients. Cumulative effects have been observed only when large doses were given as a sedative.

The danger of addiction may be less than with other hypnotic-sedative drugs, as dormison is ultra-short-acting and tends to lack their stupefying and euphorigenic action. Nevertheless, dormison should not be given as a sedative to patients who have previously been addicted to other drugs, and it should be used as a hypnotic in these cases only under hospital conditions. In view of previous reports and the authors' findings on cumulation and addiction, barbiturates should not be given to patients receiving dormison until such time as extensive data are available on the potentiating effect of dormison on barbiturates in man.

(Authors' abstr.)

Report on the Use of Succinyl Choline Dichloride (A Curare-like Drug) in Electroconvulsive Therapy.

Succinyl choline dichloride i.v. is a useful drug to produce muscular relaxation in patients receiving E.C.T. who would otherwise be poor risks because of susceptibility to fractures and pre-existing fractures. It has also proved of value in treating severely disabled cardiac patients for whom even slight exertion may be dangerous. This drug is potent and effective, but ultra-short-acting, seldom lasting more than five minutes. Artificial respiration is easily and adequately performed by standard routine methods. Oxygenation can be maintained at levels superior to that of bed rest. No untoward effects have yet been observed in over 300 electric treatments. (Authors' abstr.)

The Treatment of Tuberculous Patients with Electroshock Therapy.

From clinical experience with patients suffering from severe mental illness, aggravating and aggravated by advanced stages of pulmonary tuberculosis, the authors have no doubt about the value of electrochock therapy, and its safety, in the treatment of such patients. The results indicate that, when patients are so psychotic that they cannot co-operate in treatment for their tuberculosis, electroshock therapy may improve their mental status to the extent that they will accept treatment. The authors think some of these patients might have been successful in their suicidal attempts, or have died as a result of the tuberculosis, had it not been for the use of electroshock therapy. Moreover, there appears to be a uniformly specific improvement in the pulmonary tuberculosis following E.C.T., regardless of the stage of advancement when the treatment is started. This may be a secondary effect of electroshock therapy.

It is conjectured that electrotherapy, by hypothalamic stimulation, may alter cortical activity in such a way as to mobilize bodily defenses against various invading organisms.

All the objections to the use of electroshock treatment for tuberculous patients that Dr. Close quotes in his article were considered and discussed by the staff prior to starting treatment. Some of the staff had similar objections, but they have not been substantiated by the authors' observations, which have convinced them of the value of electroshock therapy in the treatment of tuberculous patients. (Authors' abstr.)

Measurements of Changing Psychopathology with the Minnesota Multiphasic Personality Inventory.

The M.M.P.I. is widely accepted as the best of the questionnaire-type personality tests. It is simple to administer and score, conservative of the clinician's time, well accepted by patients and provides an extensive anamnesis and a graphic indication of psychopathological status that is easy to interpret. It should not be used as a substitute for the physician's history-taking (which is so important in the early development of a therapeutic relationship), nor should it be used alone to "make" a diagnosis. With experience in the use of the M.M.P.I. characteristic profiles can be recognized as indicative of personality structure and disturbance that are not limited to diagnostic categories of any particular school. Examples have been selected to demonstrate how the M.M.P.I. can be used in measurement of changing psychopathology, thus indicating its value in analysis of clinical progress and results of treatment. (Authors' abstr.)

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A Critical Evaluation of Carbon Dioxide Inhalation Therapy in Mental Disorders.

1. The clinical, experimental, and theoretical literature on carbon dioxide oxygen inhalation therapy (C.D.T.) is reviewed and critically evaluated.

2. The over-all improvement rate in 238 nonpsychotic patients treated with C.D.T., collected from the literature, is 61 per cent. The highest rate of improvement (83 per cent.) is reported in psychophysiologic disorders, the lowest (46 per cent.) in stutterers. The evidence indicates that these high improvement rates are exaggerated since most workers include " minimal " improvement in their statistics. If these patients had been correctly classified " unimproved," the rates would be lower and much more accurate.

3. C.D.T. is apparently of little value in the treatment of psychoses, severe obsessive-compulsive, and hypochondriacal reactions.

4. C.D.T. may be a useful adjunct to psychotherapy, causing rapid release of unconscious repressed memories and affects (abreaction), thereby shortening the duration of psychotherapy.

5. C.D.T. is capable of causing amelioration of some neurotic symptoms without the use of concurrent psychotherapy. Ideally, however, C.D.T. should be combined with or followed by psychotherapy in order to induce lasting improvement in the patient through the development of insight into the cause of his symptoms and emotional difficulties.

6. No fatalities or lasting complications from C.D.T. have been reported. It is apparently the least harmful form of somatic therapy in psychiatry. However, since C.D.T. is " potentially " dangerous both physically and psychologically, it should be given only by psychiatrists or other physicians with special psychiatric training. Indiscriminate use by untrained personnel might result in serious complications.

7. C.D.T. may be of value in certain patients who are hostile to psychotherapy or who for various reasons are unable to receive other forms of treatment. Such individuals frequently become more co-operative during C.D.T., since they feel that something " active " is being done to help them and they frequently request further psychiatric treatment.

8. A major difficulty of C.D.T. is the increasing severe anxiety that it induces, which causes many patients to discontinue treatment prematurely.

9. The mode of action of C.D.T. is unknown. There is no scientific evidence that CO_2 is a specific agent in the treatment of nonpsychotic mental disorders, since many other anaesthetic agents exert similar effects.

10. Suggestions for further research are made, with particular emphasis on the need for adequate controls, prolonged follow-up studies, and physiological and biochemical analyses of the effects of C.D.T. on man and experimental animals.

(Author's abstr.)

The Factor of Hypoxemia in Electroshock Therapy.

The arterial oxygen saturation in electroshock therapy has been determined with the aid of a photoelectric oximeter. The following observations were made:—

1. Electroshock causes rather severe, but transitory, hypoxemia.
2. Impaired respiration after the convulsion can give rise to severe and rather prolonged hypoxemia.
3. If more than one shock is necessary to produce a convulsion the degree of hypoxemia is considerably increased.
4. The administration of pure oxygen for a period of ½ to 1 minute (1 minute in elderly individuals) immediately before as well as after the shock considerably reduces the degree of hypoxemia.
5. The oxygen administration prolongs the convulsion. The intensity of the convulsion is probably also somewhat increased, thus possibly increasing the risk of skeletal injuries.
6. The addition of 6 per cent. carbon dioxide to the oxygen gas is a somewhat poorer protection against hypoxia than pure oxygen. Carbon dioxide also appears to increase further the duration of the convulsions.
7. When a muscle-relaxing agent is used and oxygen insufflated, a maximum oxygen saturation of the arterial blood can be obtained throughout the treatment. The convulsion is thereby greatly prolonged. (Author's abstr.)

The Occurrence of Methemoglobinemia During Insulin Coma Therapy.

Five cases of methemoglobinemia resulting from the accidental substitution of sodium nitrite for potassium citrate in the gavage mixture given to terminate insulin coma treatment are recorded. The simple and efficacious treatment by intravenous injection of methylene blue is presented.

It is speculated that further research might show that the intentional production of methemoglobinemia in nonhypoglycemic subjects would be a safe and useful method of treatment in schizophrenia. (Author's abstr.)

Studies in Responsitivity of the Adrenal Cortex in Schizophrenia.

Eleven chronically hospitalized schizophrenic patients, in good physical and nutritional health, were studied by hourly eosinophile and lymphocyte counts after injections of saline and ACTH on consecutive days.

Wide variations in the fasting levels of these blood elements existed among different patients and in the same patients from day to day.

Saline elicited variations in eosinophile counts so that 5 of 11 subjects showed decreases of 50 per cent. or more after 4 hours. The lymphocytes varied by at least 29 per cent. for each subject at some point in the study after saline was injected.

The response of the eosinophiles to ACTH was greatest 3 hours after injection.

Ten of the 11 subjects showed a 50 per cent. or more variation in eosinophiles at some point in the procedure. All 11 subjects had more than a 50 per cent. variation in their lymphocyte counts.

The adrenal cortical response of the schizophrenics the authors have studied, as measured by the eosinophile and lymphocyte responses to ACTH and by physiological variation, falls within the normal range.

Studies of the 17-ketosteroid and corticosteroid excretion after ACTH in 11 cases of acute schizophrenia also showed varying responses in different subjects. (Authors' abstr.)

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Psychotic Reactions in Problem Drinkers Treated with Disulfiram (Antabuse).

1. Ten cases in which psychotic reactions developed during the course of disulfiram treatment are reported in detail.

2. The literature on such cases previously reported is discussed, with particular emphasis on the divergence of opinions concerning the principal etiologic factor.

3. The hypothesis is offered that the primary factor is psychogenic.

4. The importance of such distinction as it affects the treatment of patients who incur psychotic reactions is commented on.

(Authors' abstr.)

Intellectual Functions in Myxedema.

The Rorschach test was administered to three diagnostic groups: neurotic subjects, myxedematous subjects, and subjects with organic brain damage. The subjects had been individually matched in the three groups on the basis of sex, age, formal education, and intelligence quotients. Intergroup statistical comparisons were made of the mean performances on each of the Rorschach test variables. The frequencies with which scores in one group exceeded the matched scores in the other groups were tabulated and the frequency differences tested for statistical significance. The frequencies of Rorschach test "signs" of organic brain damage in the three groups were also compared statistically.

The results give a general indication that intellectual functions, as represented by the Rorschach test, suffer some impairment with myxedema. The performance of myxedematous patients falls between that of neurotic patients and that of patients with organic brain damage. In some respects their scores more closely resemble those for neurotic subjects and in others the scores for brain-damaged subjects. The specific nature of the intellectual dysfunction in myxedema was not thoroughly indicated in the present study. A greater number of subjects and a wider variety of psychological tests should be used in seeking more specific results.

(Author's abstr.)

Endogenous Eosinopenia in Institutionalized Patients with Mental Deficiency.

Eosinophile counts were obtained on institutionalized patients with mental deficiency at specified times during the morning hours on several days of investigation. Differences in numbers of eosinophiles among patients, among days of investigation, and among times of day were shown to be highly significant. It is demonstrated that a desirable experimental design will require testing of the same patients on the same days and at the same time of day. Simplification of analysis of data for changes in number of eosinophiles can be achieved by conversion of absolute counts into relative levels.

The data presented demonstrate the occurrence of endogenous eosinopenia in mentally deficient patients of both sexes. If morning changes in number of eosinophiles indicate changes in the rate of secretion of certain adrenocortical hormones, these findings support the hypothesis of a functioning adrenal cortex in the patients studied.

Endogenous eosinopenia is correlated with the initiation of daily activities in a given population. It seems necessary to adapt the schedule of sampling blood for endogenous-eosinopenia tests to the time when daily activities are routinely initiated by the subjects to be tested. (Authors' abstr.)

Study of Adrenocortical Physiology in Normal and Schizophrenic Men.

Various indices of adrenal cortex function in normal men and schizophrenic men at rest and when subjected to three stress tests (oral dextrose tolerance, pursuit meter and Target Ball Frustration tests) and to the injection of 25-mg. test doses of corticotropin are described.

The normal and psychotic groups were divided into younger (20 to 39 years) and older (40 to 60 years) groups. These four groups were studied statistically as separate populations.

In both the older and the younger groups the schizophrenic patients at rest showed a significantly higher rate of excretion of urinary water, 17-ketosteroids, sodium, and potassium than the normal subjects. They showed lower than normal rates of excretion of corticoids and phosphates and thus displayed at rest evidence both of hyperadrenalism and of hypoadrenalism.

Confirming the authors' earlier work with patients and normal subjects of the younger age group, they found that the older patients showed less adrenal response to the stress tests and to injected corticotropin than the older normal subjects. The total response index of the adrenal cortex was used in these comparisons. As in their earlier studies of the younger groups, it was the urinary 17-ketosteroids, sodium, potassium, uric acid, and inorganic phosphates that reflected these group differences. Percentage changes in eosinophile and lymphocyte levels and percentage changes in corticoid excretion, as they have previously reported, did not differentiate statistically between normal and schizophrenic populations in the four tests used.

The older schizophrenic patients, while about as unresponsive to the authors' three stress tests as the younger schizophrenic patients, were considerably more responsive to corticotropin than were the younger patients.

The experimental findings are discussed in terms of possible underlying mechanisms and in terms of their possible relation to the etiology of schizophrenia.

(Authors' abstr.)

An Extralemniscal Sensory System in the Brain.

Contrasting features of afferent conduction in the medial and the lateral corticipetal systems were studied in the brain stem and the cortex of monkeys.

Potentials in the classic lateral sensory pathways displayed rapid conduction, segregation of modality, and discrete cortical projection to primary receiving areas of the cortex.

Medially conducted potentials exhibited slower conduction, common transport for all modalities, and distribution to wide areas of the cortex by way of the diffuse thalamic projection system.

Upon peripheral stimulation, a volley of afferent impulses is conducted simultaneously to the cortex by these two systems.

The lateral system appears to subserve perception and the discriminative sensory functions, while the medial system functions in arousing consciousness or alertness, without which the above-mentioned sensory discrimination and effective response would be impossible. (Authors' abstr.)

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Cerebral Vascular Insufficiency.

It is the purpose of this paper to establish a new entity only vaguely recognized by authors in the past, namely, cerebral vascular insufficiency.

This transient condition has been demonstrated by experiment. Electroencephalograms were taken after the carotid vessels were partially or completely ligated in the monkey. When the blood pressure was lowered by bleeding the animal, focal electroencephalographic changes occurred on the side of the ligation, similar to those found in hemiplegia. When the blood pressure was restored, the electroencephalographic records returned to normal. These changes were proved to be due to a drop in blood pressure, rather than purely to anemia.

Clinically, cerebral vascular insufficiency occurs in hemorrhagic shock, coronary shock, surgical and traumatic shock, hypotension due to sympathetic block, and Smithwick sympathectomy, postural hypotension, carotid sinus stimulation, spinal anesthesia, and cardiac surgery. It also can occur as a result of miscellaneous extracranial factors, such as surgical ligation of the carotid arteries, spontaneous thrombosis of the internal carotid artery (Denny-Brown syndrome), gravitational states, as in flying, and the use of antihypertensive drugs. The changes which occur are transient if the blood pressure is restored to normal within a short period. The electroencephalographic changes and symptoms of cerebral origin, such as hemiplegia and hemianesthesia, will then usually disappear. If the blood pressure is not promptly restored to normal in patients with cerebral arteriosclerosis or congenital anomalies, focal changes will be permanent. As in the heart in which coronary arteriosclerosis has occurred, it is important to maintain the cerebral blood pressure at normal levels, especially in the elderly patient with narrowing of cerebral arteries.
(Authors' abstr.)

Cutaneous Perception in the Aged.

Tests of double simultaneous tactile stimulation, particularly the face-hand test, were performed on 342 normal adults of ages varying from 40 to 96.

Thirty-six per cent. of subjects 40 to 65 years of age made perceptual errors in the initial test, but nearly all these correctly perceived both stimuli during subsequent trials.

The perceptual errors consisted of extinction or displacement of one of the two stimuli. This phenomenon occurred in a pattern in which the face was dominant to the hand and the foot dominant to the thigh.

Of the group 65 to 96 years of age, 96 per cent. showed errors on the initial trial, and 54 per cent. persisted in their errors after 10 trials of tests. The incidence of persistent errors in this group increased with increasing age.

This relation of age to persistent errors in the very old subjects is similar to that demonstrated in normal children under 6 years of age; the younger the child, the greater the incidence of persistent incorrect responses. Perception of double simultaneous stimuli in the normal subject is therefore most faulty at the beginning and the end of the life span, but the causes of the changes in each group must be different.
(Authors' abstr.)

Cardiovascular Changes Associated with Electroconvulsive Therapy in Man.

The arterial blood pressure response to electroconvulsive therapy in man followed a pattern similar to that observed in dogs and monkeys subjected to electroconvulsive shock. Since it was found that the cerebral blood flow pattern duplicated the blood pressure pattern following electroconvulsive shock in animals, it is assumed that unless a different relation between blood flow and blood pressure can be demonstrated in man than exists in these animals, the cerebral blood flow response in man should follow the same pattern as the blood pressure response to electroconvulsive therapy.

The blood-pressure response to electroconvulsive therapy in man exhibited an initial decrease below control levels during the early tonic phase, followed by a marked elevation above the control level during the late tonic and throughout the clonic phase of the convulsion. The blood pressure began to decline while the convulsion and the respiratory arrest continued ; a secondary decrease below control pressure was reached shortly after the end of the convulsion, and this was followed by a secondary increase to a peak above the control level within two minutes after shock. The arterial pressure then decreased gradually, returning to the control level, or remaining only slightly above or below that level within 20 to 30 minutes after shock. This general pattern of response was found in 31 treatments evoking a major reaction to electroconvulsive therapy, in 4 treatments administered to fully curarized patients who gave evidence of a major reaction to electroconvulsive therapy, in 28 subconvulsive treatments, and in a subconvulsive shock treatment given one fully curarized patient.

The similarity in the blood-pressure response patterns in the three groups of patients, namely, patients showing major reactions, patients having subconvulsive reactions, and fully curarized patients, indicates that the cardiovascular changes following electroconvulsive therapy are independent of the convulsions and appear to result from the effects of the electroshock stimulus alone.

The marked and prolonged elevation in arterial pressure following the onset of the shock stimulus indicates a marked increase in cerebral blood flow during this time, thus making it improbable that extensive cerebral vasoconstriction occurs.

No correlation was found between the pretreatment level of blood pressure and the height of blood-pressure elevation during electroconvulsive therapy.

During the convulsion, diastolic pressure exhibited a greater percentage increase than did systolic pressure.

It appears that curare (tubocurarine) *per se* does not produce marked changes in blood pressure in man. (Authors' abstr.)

Cardiovascular Changes Associated with Electroconvulsive Shock in Monkeys.

The immediate effects of electroconvulsive shock on the internal carotid blood flow, arterial pressure, and cardiac rate were recorded in experiments on a series of 10 monkeys under light chloralose anesthesia. The shock stimulus, in terms of milliamperage, voltage and duration of current, was also recorded.

Blood flow was measured continuously in the internal carotid artery by the use of an electromagnetic blood-flow meter. By the use of a Statham gage-Offner recorder system, blood pressure was measured directly and continuously at the same site as was blood flow. Changes in cardiac rate were obtained from the pressure records.

The initial response to electroconvulsive shock were convulsions, respiratory arrest, bradycardia, and reduced cerebral blood flow and arterial pressure ; the last three responses had a duration of one to three seconds. This initial decrement in blood flow, blood pressure, and cardiac rate was followed by a pronounced increase above control levels, which reached a peak during the clonic phase of the convulsion. Blood flow and arterial pressure reached their highest elevations concomitantly ; and then, while the convulsion and respiratory arrest continued, they began to decline. The lowest point of this secondary decline was reached a few seconds after the end of the convulsion. Blood flow and blood pressure then exhibited a secondary rise, which reached peak elevations one minute after shock. Blood flow and blood pressure then began a gradual decline until, 30 minutes after shock, blood flow and arterial pressure in a majority of the 10 animals had returned to control levels. After the initial decrease and increase following electroconvulsive shock, the cardiac rate exhibited a gradual, but erratic, decline toward control levels ; control levels were reached by a majority of the animals within 30 minutes after shock. At the cessation of the seizures the monkeys exhibited a prolonged cardiac arrhythmia, of several minutes' duration.

This study on monkeys supports the conclusions drawn in a previous work on dogs that changes in blood flow in the carotid artery appear to be a passive response to marked changes in arterial pressure. Because of the pronounced elevation which occur in blood flow and arterial pressure during the convulsions in monkey subjected to electric shock, support is also given to a previous contention that cerebra ischemia resulting from cerebral vasoconstriction is not of functional significanc in electroconvulsive shocks. (Authors' abstr.)

Incidence of Alzheimer's Disease in a Large Mental Hospital.

Histologic studies by means of silver techniques were carried out on the brains of 210 patients in an attempt to correlate the recorded clinical changes with the pathologic alterations. As a concomitant of the widespread formation of argyrophilic plaques and neurofibrillary changes, a definite clinical picture emerged from the survey. This semeiotic pattern was remarkably consistent regardless of the age of onset of the mental symptoms. It is characterized by slowly progressive intellectual deterioration. Restless wandering, particularly at night, is characteristic ; later, when motor activity becomes restricted, there is aimless picking at objects in the immediate environment. Verbal output decreases, and " aphasia" ensues when primary speech and speech associated areas are involved. Other neurologic signs, such as forced grasping and pseudobulbar paralysis, are late concomitants. The clinical picture may appear at any age ; there is no relation between the severity of the pathologic process and the age at which mental signs are first manifested.

Argyrophilic plaques and neurofibrillary changes are not characteristic of old age *per se.*

Since there is no difference in the clinical or pathologic picture in the various age groups, the postulation is made that Alzheimer's disease is a specific entity, and not a " presenile " dementia. (Authors' abstr.)

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Language Behavior in Psychoneurotic Patients.

The focus of this paper is mainly on the study of language as an available objective tool for validation and exploration of psychological traits. The present study suggests that this is possible and that certain characteristics of language behavior point to parallel characteristics in psychological make-up. A descriptive evaluation is given of the language behavior of a subgroup of the psychoneuroses (hysteria) as distinct from that of the " normal " pattern. It appears from the authors' findings that the language pattern of " neurotic " patients shows a significant relative increase in the use of verbs and pronouns and a significant relative decrease in the use of substantives, adjectives, prepositions, conjunctions and articles. In the 10 most frequently used words, " neurotic " language patterns differ from " normal " patterns in the use of the pronouns " it " and " you " and in substitution of " is " for " was." The incidence of the pronoun " I " is significantly higher in " neurotic " language. Significantly fewer different words are used per thousand.

(Authors' abstr.)

Psychodynamics in the Excessive Drinking of Alcohol.

In the present state of knowledge, it would appear that the symptom of excessive drinking of alcohol and addiction to alcohol are the products of various social and biological forces. This paper is concerned predominantly with a scrutiny of the individual psychological factors. For specific reasons the particular framework of the theoretical discussion is that generally outlined by psychoanalytic theory. In the introductory section the most widely applied psychodynamic hypothesis is summarized. In brief, this emphasizes the importance of oral drives in the motivation to drink excessively. The purpose of this paper is to present a revised hypothesis which, in essence, suggests that drinking and intoxication can be put in the service of psychic defense mechanisms against various sources of anxiety. The author's case material does not support a generalization that the immediate source of the anxiety is oral conflict. Instead, the anxiety being assuaged by the drinking appears to vary from one person to another. However, as the drinking episodes continue, the " pleasure " obtained from the intoxication can begin to supersede as goal the relief from the original anxiety. Ultimately, the psycho-dynamic conflict specific to the outset of the problem may come to be overshadowed by the " nonspecific " oral narcissistic elements. (Author's abstr.)

Thiamylal in Electroconvulsive Therapy and Significance in Analysis of Seizure Mechanisms.

1. A series of 20 patients receiving both electroshock and thiamylal (surital) sodium preceding the electroconvulsive treatment is reported.

2. Thiamylal changes the seizure by shortening its duration and prolonging the post-seizure apnea.

3. The total period of apnea tends to remain constant in treatment both with and without thiamylal.

4. Thiamylal given prior to electroshock helps in preventing pretreatment apprehension and postconvulsive excitement.

5. Psychiatric improvement of patients receiving thiamylal-electroshock therapy was essentially that expected after treatment with ordinary electroconvulsive therapy.

6. A theory is proposed stating that the peripheral convulsion in electroshock is independent of the respiratory arrest and that these two phases are mediated through different brain centers. Data are presented in support of this theory.
(Authors' abstr.)

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Clinical Significance of Sclerosis of the Cornu Ammonis.

The brains of 50 institutionalized epileptic patients were examined and their clinical records reviewed, with special emphasis on the presence or absence of ictal " psychic phenomena." The results are summarized as follows :

1. In 29 cases there was sclerosis of the cornu ammonis. These cases were classified as follows : Group A, sclerosis of the cornu ammonis without other remarkable changes, 9 cases ; Group B, frontal or frontotemporal traumatic lesions, in addition to the sclerosis of the cornu ammonis, 9 cases ; Group C, congenitally malformed brains, 11 cases. Sclerosis of the cornu ammonis was unilateral in Groups A and B and bilateral in Group C. In nine cases of Group A and in seven cases of Group B ictal psychic phenomena were exhibited, a prominent feature of which was rage. The incidence of emotional changes between attacks was high in these groups. The cases of malformed brains were not considered in the clinical evaluation because of the severe mental deficiency.

2. In 21 cases there was no sclerosis of the cornu ammonis. These were subdivided as follows : Group A′, no cerebral changes, five cases ; Group B′, temporal or frontotemporal traumatic lesions, nine cases, and Group C′, malformed brains, seven cases. Ictal psychic phenomena and emotional changes were not observed in Group A′ and were seen in only three cases of Group B′. The phenomenon of rage was observed in only one of the latter cases.

3. The electroencephalograms, obtained in a few of the cases, showed a spike or sharp-wave focus predominantly in the anterior temporal region on the side of sclerosis of the cornu ammonis.

The possible rôle of the hippocampal formation in psychomotor epilepsy or temporal-lobe automatism is discussed. (Authors' abstr.)

Effects of Aging on Cerebral Circulation and Metabolism.

Cerebral blood flow and metabolism were measured by the nitrous oxide method in 32 normal men between the ages of 38 and 79 years and the data compared with those obtained in previous similar studies on 19 normal subjects between the ages of 18 and 36 years.

There is a close statistical correlation between advancing age and decreasing cerebral blood flow and increasing cerebral vascular resistance. The reduction in cerebral blood flow and increase in cerebral vascular resistance are accelerated after middle age. Cerebral oxygen consumption remains fairly stable until after middle age, when it apparently begins to decrease with advancing age.

The reduction in cerebral blood flow and increase in cerebral vascular resistance are thought to be due to increased cerebral vascular tone and vascular sclerosis. Diminution in cerebral oxygen consumption is thought to result from impaired cellular function resulting from reduced blood flow.

In eight of the subjects inhalation of a mixture of 10 per cent. CO_2 and 90 per cent. O_2 resulted in apparent increases in cerebral blood flow of more than 100 per cent.; indicating that the increased cerebral vascular resistance of the aged is not necessarily fixed. (Authors' abstr.)

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A Familial Evaluation of the Electroencephalogram of Patients with Primary Behavior Disorder and Psychopathic Personality.

1. E.E.G.s were recorded from patients diagnosed primary behavior disorder or psychopathic personality (N = 86) and their true parents (N = 172). E.E.G.s were recorded from 9 other patients and both of their foster parents (N = 18). All patients were carefully screened and none, *on the basis of clinical evidence,* had epilepsy, psychoneurosis, functional or organic psychosis, or sequelae of a physical illness or injury. No patient had an I.Q. below 80.

2. Fifty-four per cent. of the patient group exhibited E.E.G.s outside the normal range. Most of the abnormalities fell in the *slow* range.

3. The true parents of the patient group showed a slight decline in the proportion of normal E.E.G.s when compared to Gibbs' normal control group. In the group of true parents, only 69·8 per cent. were normal while 30·2 per cent. were abnormal. These also tend to show a greater percentage of abnormality in the *slow* group.

4. There was a statistically significant trend indicating that the patients with slow E.E.G.s had parents with slow E.E.G.s, and the patients with fast E.E.G.s had parents with fast E.E.G.s.

5. No meaningful relationship appeared between the E.E.G.s of foster-children and foster-parents.

6. It is proposed that (non-diagnostic) E.E.G. abnormalities in primary behavior disorder and psychopathic personality have important genetic determinants.

(Authors' abstr.)

The Electroencephalogram During Hypoxia and Hyperventilation.

1. The frequences in the electroencephalogram were not tangibly altered by inhalation of 6·5 per cent. oxygen in nitrogen when the gas mixture contained 4·5 per cent. carbon dioxide for stabilization of the carbon dioxide content of the blood.

2. Standardized hyperventilation with carbon dioxide free media of varying oxygen content was compared with hyperventilation with room air. Pure oxygen gas diminished the effect to half. Nine per cent. oxygen in the inspired gas increased the effect threefold, and 7·5 per cent. oxygen eightfold.

3. In the tests mentioned in point 2, there was no significant difference in reaction between the patients who had recently undergone electric shock treatment and the epileptic patients. It was shown that the spontaneous spike and wave activity in the resting E.E.G. of epileptic patients can be increased threefold by

hyperventilation with oxygen, eightfold by hyperventilation with air, and fifteenfold by hyperventilation with 9 per cent. oxygen.

4. Variations in the pulse rate paralleled on the whole variations in the E.E.G. The more slow activity in the E.E.G. the higher was the pulse rate.

5. The mental activity was frequently considerably impaired during hyperventilation with a low oxygen medium.

6. In all hyperventilation tests age had a significant influence. In subjects below the age of 25 even hyperventilation with air had a pronounced effect, while in those over the age of 40 there was usually no reaction even to hyperventilation with low oxygen mixtures.

7. In the clinical tests it was shown that hyperventilation with oxygen-poor medium can be used as a complement to the usual hyperventilation test. The method provides less risk of the abnormal cases being overlooked, and could probably be used as an additional criterion for normality.

8. The main theories concerning the cerebral mechanisms during hyperventilation and hypoxia are discussed. It is assumed that hypocapnia is probably the essential factor which produces slow waves in the E.E.G. during hyperventilation. Hypoxia gives a strong support but is unable to produce any such effect without co-existing hypocapnia. (Author's abstr.)

Studies on the Mechanism of the Action of Visual Afferents on Motor Cortex Excitability.

1. The growing interest in the effect of sensory stimulation and especially of light stimulation on epileptic and myoclonic phenomena raises two questions of particular importance. The first is whether light stimulation produces its effect on the motor system by affecting the motor cortex or whether the effect is injected into the motor system at lower levels. The second question is by what pathways the visual afferent impulses reach the motor system in order to affect its threshold. A study of these two questions has been carried out on 30 cats under various types of anaesthesia including chloralose and semicarbazide. In order to test the excitability of the motor cortex, bipolar stimulating electrodes were placed on it and recording electrodes were placed in the pyramidal tract at the medullary pontine junction. The height of the response recorded from the pyramidal tract was used as an index of motor cortex excitability.

2. The response recorded from the pyramidal tract after a single stimulus to the motor cortex is a complex one of prolonged duration. The authors' analysis of the pyramidal discharge suggests that it contains two sharply differentiated components. The fast component is probably due to direct stimulation of cells and perhaps fibres which contribute directly to the pyramidal tract (D response). The second slow component (I response) is probably due to stimulation of internuncial cortical cells which fire onto cells whose fibres contribute to the pyramidal tract.

3. The effect of a single light flash in the eye or of lateral geniculate electric stimulation is to produce a prolonged period of facilitation of the motor cortex. In some animals the light flash alone produces a descending volley in the pyramidal tract. It is concluded that the light flash affects both the cortical cells of origin of the pyramidal tract and the cortical interneurons. Some preliminary evidence suggests that other sensory systems may produce a similar phenomenon.

4. It is shown that the effect of visual afferents on the excitability of the motor cortex is unaffected by complete removal of the occipital lobe cortex. It is concluded that neither the primary visual receiving area nor the visual association area need be present for the facilitating effect of visual stimulation to occur in the motor cortex.

5. Complete removal of the cortex of the superior colliculus did not affect the time course or size of the facilitating effect of a visual afferent volley on the excitability of the motor cortex.

6. Lesions placed in the pretectal region abolished the facilitatory effect of visual stimulation.

7. It is therefore concluded that neither of the two main visual projection systems are responsible for the facilitatory effect of visual afferent volleys on the motor cortex. The possible rôle of other visual pathways, especially the ventral division of the lateral geniculate (the pregeniculate system) is discussed.

(Authors' abstr.)

Effect of Malononitrile upon the Electrocorticogram of the Rabbit.

The effect of malononitrile injection on E.C.G., evoked visual response and steady potential across the cortex was studied in 14 rabbits carried under minimal anesthesia.

1. After injecting 10 to 25 ml. of 1 per cent. malononitrile intravenously the first changes noted in cortical activity included the development of slow waves in E.C.G., loss of the negative phase of the evoked visual response, and exaggeration of its positive after-effect component. Thereafter the steady potential across the cortex underwent a gradual positive shift, the E.C.G. became isoelectric, and the positive phase of the evoked response diminished in amplitude progressively until the animal died 5 to 8 minutes later.

2. Sodium thiosulfate can reverse this process, attributable to cellular anoxia, if its injection is commenced sufficiently early. The injection must be started at the time when slow waves are commencing to appear in E.C.G., the negative phase of evoked response has just disappeared, and the positive after-effect component has become exaggerated. The reversal of effect takes time, and in one or another aspect, further deterioration is to be expected after the injection of sodium thiosulfate is started. Eventually, however (5–8 min.), with injection of about 20 ml. of 5 per cent. sodium thiosulfate, the preinjection state for malononitrile may be completely restored. (Authors' abstr.)

On the Physiological Action of Carbon Dioxide on Cortex and Hypothalamus.

Inhalation of 10 per cent. CO_2 reduces the responsiveness of specific sensory projection areas to optic and acoustic stimuli while it increases the reactivity of the hypothalamic-cortical system. The activation of the latter is evident from the increased asynchrony of potentials in all parts of the cerebral cortex which is associated with similar changes in hypothalamic potentials. In sensitive preparations and/or under the influence of slightly higher concentrations of carbon dioxide neuronal recruitment may occur resulting in a marked increase in the amplitude of the potentials. This effect of carbon dioxide on the hypothalamic-cortical system is similar to that produced by proprioceptive or nociceptive stimuli which evoke arousal reactions in lightly anesthetized animals. It is shown that the action of proprioceptive and nociceptive stimuli is greatly magnified in hypercapnia.

The excitability of the cortex is thought to depend, other conditions being equal, on the hypothalamic-cortical system which influences the cerebral cortex as a whole and afferent impulses whose action is confined to a specific cortical projection area (optic stimulus → visual cortex). A functional separation of these two systems can be achieved by the action of carbon dioxide.

The effect of high concentrations of carbon dioxide (30 to 40 per cent.) administered in oxygen or air is fundamentally different from that of "low" carbon dioxide. The chief actions of "high" carbon dioxide are :

It reduces or eliminates the small, frequent background potentials while the grouped, Dial potentials are relatively unchanged. If high carbon dioxide is administered for longer periods cortical activity may temporarily disappear. Thereafter, Dial potentials reappear and may occur more frequently than prior to the administration of carbon dioxide. Topically induced cortical strychnine spikes undergo a slight reduction in amplitude and a marked diminution in frequency under the influence of high carbon dioxide concentrations.

Potentials recorded from the posterior hypothalamic area show similar changes. The reduction in amplitude and frequency of the potentials suggests neuronal decruitment in cortex and hypothalamus under the influence of anesthetic carbon dioxide concentrations.

The potential changes described in the preceding paragraphs occur in carbon dioxide-air as well as in carbon dioxide-oxygen mixtures. They are reversible on readmission of air. Occasionally, rebound phenomena are observed under these conditions.

Optic and acoustic stimuli still elicit typical responses in their specific cortical projection areas even when the resting potentials of these or other parts of the cortex have vanished. The reduction in amplitude of the acoustic potentials is less than that of the visual cortical responses.

While specific cortical projection areas remain excitable in high carbon dioxide, the generalized response of the whole cerebral cortex to proprio- and nociceptive stimuli is abolished. Since hypothalamic excitation is likewise missing, this result is interpreted as indicating that " high " carbon dioxide eliminates the reactivity of the hypothalamic-cortical system while the responsiveness of specific cortical projection areas is retained.

It is suggested : (*a*) that the selective functional elimination of the hypothalamic-cortical system, which is activated in arousal, is characteristic for the state of loss of awareness and narcosis ; (*b*) that the background potentials of the cortex depend primarily on hypothalamic-cortical discharges ; (*c*) that functional elimination of the activating hypothalamic-cortical system releases the inhibitory system regulated by intralaminar thalamic nuclei and leads to more frequent dial potentials in the cortex. (Author's abstr.)

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Five-year Follow-up in One Hundred Cases of Bilateral Prefrontal Lobotomy.

The first 100 patients treated at the Boston Psychopathic Hospital with bilateral prefrontal lobotomy, or the standard operation as developed by Dr. James L. Poppen, were followed five years after the operation. Forty patients were residing in the community and 45 in hospitals, 12 had died, and 3 could not be traced.

Twenty-nine per cent. of the patients on whom information was available were considered to be making a " good " work adjustment five years after operation ; that is, they were earning a salary and their performance apparently satisfied their employers. If engaged as housewives, they were working full time and satisfactorily, as far as their relatives were concerned. In contrast, only 2 per cent. of the patients were considered to have had good work adjustment preoperatively, and 66 per cent. were considered to have had good work adjustment before their illness began.

Comparison of the adjustment five years postoperatively with that shown from 1 to 4 years postoperatively indicated that improvement after surgical treatment was generally maintained over five years. For the average patient, there was no significant deterioration of adjustment. Postoperative improvement generally was not up to the level of adjustment enjoyed by the patient before illness began, although it was considerably higher than the level of adjustment during illness and before operation. The operative mortality was 2 per cent. (Authors' abstr.)

Effects of Ethyl Alcohol on Cerebral Blood Flow and Metabolism.

The cerebral blood flow, cerebral metabolism, and cerebral vascular resistance were measured in 15 subjects before and during intravenous administration of ethyl alcohol and in 12 patients during and after severe self-induced alcoholic intoxication. The administration of ethyl alcohol in doses sufficient to produce facial vasodilatation and the mental changes of mild inebriation produced no changes in cerebral blood flow, cerebral metabolism, or cerebral vascular resistance. During acute severe alcoholic intoxication, there was a pronounced increase in mean cerebral blood flow, an equally significant reduction in cerebral oxygen uptake, and a reduction in cerebral vascular resistance, as compared with the values obtained following recovery. Low concentrations of alcohol in the blood (averaging 68 mgm. per 100 c.c.) had little or no measurable effect on cerebral circulation, while high levels (averaging 320 mgm. per 100 c.c.) produced a pronounced depression in cerebral oxygen consumption, despite an increase in blood flow. There appears to be no rational basis for the use of ethyl alcohol as a vasodilator in patients with cerebral vascular disease. (Author's abstr.)

Management of Nocturnal Enuresis by Conditioned Response.

Treatment of a group of 42 patients with chronic nocturnal enuresis by development of a conditioned response is described. All patients, after examination to rule out organic lesions as a cause, were treated by being awakened immediately after the commencement of nocturnal urination by an automatic electric alarm. The purpose of this procedure was to condition them to awaken instead of urinate in response to bladder tension. All patients had resisted a variety of treatment methods previously. Enuresis was arrested in 38 (90·5 per cent.) of 42 patients, and the majority of these patients eventually learned to sleep through the entire night ; five required a second treatment after reversion, and in four the treatment was unsuccessful. Parental co-operation is of primary importance for success in the case of young children, and lack of it is the commonest cause of failure ; hence, professional supervision is an important feature of the treatment. Personality difficulties improved considerably in the majority of patients, indicating that such maladjustments may often be the effect, rather than the cause of enuresis. The conditioned response management of enuresis appears to offer a positive method of attack on a common and stubborn affliction and its attendant personality difficulties. (Author's abstr.)

Methods of Treatment of Delirium Tremens.

From the literature only one factor is common to the various methods of treatment of delirium tremens ; that is, regardless of the method previously employed, when a physician becomes interested in the syndrome, his results are approximately 50 per cent. better, as measured by morbidity and mortality, than the results obtained in the patients selected for a control series. Piker's excellent work showed that regardless of the presence of hydration or dehydration, spinal drainage or no spinal drainage, and use of digitalis or no use of digitalis, neither the morbidity nor mortality in delirium tremens was significantly affected. Therefore it would seem that, regardless of the approach used, the results of treatment will be enhanced if the patient is closely observed during his state of delirium and if he receives adequate care for his systemic difficulties.

It is advocated that the usually evident systemic dehydration be relieved by the administration of sufficient fluid either orally or parenterally and that the patient's hypochloremia be alleviated by giving sodium chloride. The liver glycogen as a rule is depleted; therefore glucose is needed and alcohol is contraindicated. An adequate dietary intake supplemented by a sufficient amount of vitamins to cover the daily requirement and the deficiency that has occurred as a result of the preceding alcoholic bout should be provided. Restraint should be avoided if possible. The delirium is best controlled by paraldehyde, chloral hydrate, and the long-acting barbiturates in that order of preference. Adrenal cortex extract or corticotropin may be included if the patient has cirrhosis or fails to respond to the routine described.

The following outline of treatment is suggested for uncomplicated delirium tremens or for the delirious states that develop in alcoholics postoperatively, during a systemic illness, or following trauma. 1. To 1,000 c.c. of 5 per cent. glucose in isotonic sodium chloride solution should be added 500 mgm of ascorbic acid, 200 mgm. of thiamine, and 100 mgm of nicotinic acid or some vitamin preparation containing an equivalent amount of vitamins. This solution should be given twice in the first 12 hours; if there is evidence of cardiac embarrassment the diluent for the second infusion should be water rather than isotonic sodium chloride solution. 2. Paraldehyde should be administered, with 10 to 16 c.c. orally as an initial dose, depending on the degree of delirium, followed by 8 to 12 c.c. orally each hour as necessary to control the delirium; this is usually accomplished by the fourth or fifth hour. 3. Chloral hydrate, 2 gm. initially and 1 or 2 gm. every three hours may be substituted if the patient refuses to take paraldehyde. 4. Mephobarbital (mebaral ® 6 grains (0·4 gm.)) initially and 3 gr. (0·2 gm.) four times a day, should be given to supplement the other sedatives; after 48 hours, the mephobarbital alone should suffice for sedation. (Author's abstr.)

Hazards of Lobotomy.

The hazards during operation and undesirable sequelae of prefrontal lobotomy (702 operations) and transorbital lobotomy (1,303 operations) are discussed. While there is slightly higher risk of fatal hemorrhage in transorbital lobotomy, the incidence of other causes of operative fatality are so low that the mortality is only half that for prefrontal lobotomy. Long-term follow-up in the series of patients treated by prefrontal lobotomy by the authors shows a wide distribution of causes of death not linked with operation. There is a preponderance of deaths from heart disease. On the other hand, in the transorbital lobotomy series a larger number of late deaths are attributable to malignant disease. The explanation lies in the fact that transorbital lobotomy is an effective palliative measure for the pain and suffering of the terminal cancer patient, while prefrontal lobotomy is too drastic a measure for this purpose. Physical complications, such as hemiparesis, seizures, and incontinence, are 10 times as prevalent after the major operation as after the minor transorbital operation. Socially undesirable traits also are 10 times as common after prefrontal lobotomy as after transorbital lobotomy. Because of the high incidence of fatalities and complications following prefrontal lobotomy, the use of this procedure has been almost abandoned in the past three years. Transorbital lobotomy, on the other hand, has become the method of choice. The hazard of delay is an important one in lobotomy of any kind. Chronic mental disorder is a serious handicap to social readjustment of the patient who has undergone lobotomy. (Author's abstr.)

Significance of Grand Mal *Seizures Developing in Patients over Thirty-Five Years of Age.*

The records of 125 ambulatory men who had had *grand mal* seizures starting at or after 35 years of age were reviewed. The seizures had been recurring for from

6 months to 29 years. These patients had no significant abnormalities in their neurological status, spinal fluid or roentgenograms of their skull at the onset of the seizures. Fifty-three per cent. were observed four or more years after the onset of the seizures without showing evidence of progressive degeneration or destructive lesion of the brain. Only 5 out of 58 patients given psychological tests showed evidence of structural brain disease on these tests. Four other patients showed similar disturbances during the clinical mental status examinations.

Hypertension, severe closed head injuries, and alcoholism contributed to the development of seizures in 32·5 per cent. of these patients. No brain tumors were detected in this group, although 53 pneumoencephalograms and 3 ventriculograms were made. They revealed only four atrophic lesions resulting from head injuries, intractable seizures, and one cerebral thrombosis that occurred 14 years after the onset of seizures.

About 85 per cent. of patients who have had seizures due to brain tumors have had either Jacksonian seizures or other indications of a focal lesion within one year after onset of the seizures Less than 10 per cent. of brain tumors will cause *grand mal* seizures for more than one year without abnormalities in the clinical, spinal fluid, or skull roentgenographic examinations. At that stage in the development of a brain tumor when *grand mal* seizures are the only indication of a tumor, it seems unlikely that the present diagnostic procedures of pneumoencephalography, ventriculography, and arteriography will reveal the tumor. These patients will have to be carefully followed to detect any change in their findings before a space-occupying lesion can be detected. Although patients in whom *grand mal* seizures develop late in life should be carefully investigated and followed to determine the basis of the seizures, it should be recognized that in at least 50 per cent. of patients who have *grand mal* seizures without other abnormal findings, no destructive lesion of the brain will develop, and they will have a long course without cerebral deterioration.

(Author's abstr.)

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Cellular Pathology of the Nucleus Basalis in Schizophrenia.

1. The large nerve cells of the nucleus basalis (in the substantia innominata) have been examined in normal adult brains, in 10 brains of very old but otherwise normal people, and in 9 patients diagnosed as schizophrenic.

2. While only senile changes were present in the senile brains, many of the large cells in all of the schizophrenic specimens were found reduced in size. The smallness was interpreted as being of congenital origin and termed "dwarfism."

3. A considerable number of the cells in the schizophrenic group showed various additional changes, such as swelling, shrinkage, disappearing cell bodies, accumulation of lipofuscin, coarse fatty vacuolization, glassy appearance, and liquefaction.

4. These changes were clearly acquired during life, possibly as a result of the congenital dwarfism. The latter may have caused autonomous regression or increased susceptibility to various pathogenic agents.

5. The last four of the cell changes mentioned resembled those observed in the senile brains. As yet it would be unjustified to identify these changes with premature ageing. (Author's abstr.)

Cerebral Injuries Caused by Atomic Bombardment.

Among the casualties of atomic bombing 37 brains were examined. More or less severe changes were found in 32 of them.

Two groups may be distinguished: the first showed changes due to circulatory disturbances comparable to those which have been described as the result of excessive doses of radium and roentgen radiation. The authors' material, however, showed certain deviations from the known forms of radiation damage.

The difficulty of establishing a specific pathogenic pattern in view of the most complex conditions of exposure is emphasized.

The second group showed severe selective changes and even destruction of nerve cells. Their pathogenesis is discussed. (Authors' abstr.)

Cerebral Pedunculotomy for the Relief of Involuntary Movements. II. Parkinsonian Tremor.

1. The results of approximately a three-year follow-up of 4 cases treated by cerebral pedunculotomy for parkinsonian tremor are presented.

2. The tremor may be abolished temporarily or permanently by the operation, but at the expense of a certain degree of now predictable paralysis.

3. Tremor returning after operation may be more amenable to antispasmodic drugs.

4. The manifestations of the parkinsonian syndrome, other than tremor, are little, if at all, affected by the operation.

5. Patients should be rigidly selected for operation.

(Author's abstr.)

Reversible Cortical Blindness Following Occipital Electric Shock Treatment.

1. Six cases of transient cortical blindness following electric shock are described. Blindness occurred with electrodes in no other position than the occipital. The incidence was 12·5 per cent. (5 out of 40 patients) after abortive seizures, and 2 per cent. (1 out of 50 patients) after full-scale seizures.

2. Blindness ranged from an experience of opaque gray to complete darkness, and usually cleared after one to ten minutes. One patient, however, recovered only after four hours, allowing detailed examination yielding evidence of an optic agnostic disorder.

3. Recovery occurred either gradually, step by step in sudden leaps, or in a labile manner, defective vision alternating with moments of intact visual acuity. These patients showed central scotomata during recovery.

4. The perceptual defects were not part of a generalized postconvulsive disturbance but were restricted to occipital cortical function. Four cases showed a distortion of time experience ; this was of the " slow motion " type.

(Author's abstr.)

The Tonic Plantar Reflex and Its Localizing Significance.

1. In eliciting the plantar reflex attention should be given to intensification of the response.

2. The tonic plantar reflex is characterized by a slow contraction of the toes and distal part of the foot induced by stimulation of the sole of the foot. The contraction persists for 1 to 2 minutes, whereupon the toes and distal part of the foot return, equally slowly, to their previous position.

3. The tonic plantar reflex should be distinguished from the exaggerated plantar reflex and from voluntary, persistant flexion of the toes. In the exaggerated plantar reflex, the contraction occurs more rapidly and is brisker than in the tonic plantar reflex.

4. The tonic plantar reflex is not identical with the grasp reflex because it often occurs in the absence of the grasp reflex.

5. The tonic plantar reflex indicates the presence of a lesion of one or both frontal lobes, chiefly in their posterior part. The reflex may be homolateral, contralateral or bilateral with respect to the frontal lesion.

6. The occurrence both of a tonic plantar reflex and a grasp reflex is presumably indicative of a homolateral lesion.

7. In the presence of a bilateral tonic plantar reflex, the side on which it is most intense is presumably homolateral to the lesion.

8. Equal tonic plantar reflexes on the two sides are presumed to indicate a lesion of the corpus callosum.

9. When a unilateral tonic plantar response is accompanied by a contralateral Babinski phenomenon or other pyramidal sign the tonic plantar reflex is homolateral to the lesion.

10. Damage to the frontal extrapyramidal connections, the functions of which are predominantly homolaterally exerted, is presumably the underlying cause of the tonic plantar reflex.

(Author's abstr.)

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Response of Serum Citric Acid Levels in Schizophrenics to the Intramuscular Administration of Insulin.

1. Serial serum glucose and citric acid levels were performed on 12 male adult schizophrenics after the intramuscular administration of 20 units of insulin.
2. Seven of the 12 cases showed an abnormal response to insulin. The hypothesis is advanced that this abnormal response was due to an excessive secretion of epinephrine which neutralized the action of the administered insulin.
3. Serum calcium, glucose and citric acid levels were performed on 26 adult male schizophrenics before and after the administration of 80 to 300 units of insulin.
4. Twenty of the 26 cases showed a lowering in the serum citric acid, while the other 6 cases showed either no change or a rise in the serum citric acid. Here, too, the hypothesis is advanced that the results obtained in the above 6 cases were due to an excessive secretion of epinephrine.
5. Calcium levels remained within normal limits and were essentially unchanged after insulin administration. (Authors' abstr.)

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Cortical and Subcortical Electrical Activity in Experimental Seizures Induced by Metrazol.

An electroencephalographic study has been made of both cortical and subcortical activity occurring in the brain of the cat during seizures produced by convulsive doses of metrazol and by auditory stimuli or direct stimulation of thalamic nuclei in the presence of subthreshold doses. The effect upon this activity of various lesions was also observed.

The seizure induced by threshold doses of metrazol appeared, by every test, to be primary in the cerebral cortex and to radiate from it to deep structures. Prominent activity in the internal capsule, basis pedunculi, subthalamus and midbrain tegmentum appeared to represent discharge descending to motor outflows. The basal ganglia did not display conspicuous seizure activity. The thalamus was prominently involved, its sensory relay nuclei exhibiting the most marked seizure discharge, paralleling that in related cortical areas. Associational thalamic nuclei were next most affected. The nuclei of the diffuse thalamic projection system were implicated later than their neighbors and manifested a markedly different type of activity, resembling giant spindle bursts. The possibility is suggested that this may be associated with loss of consciousness in seizures.

With subconvulsive doses of metrazol, repetitive afferent stimulation led to development of a complex evoked potential in the receiving cortex, to its irradiation to other cortical area and, finally, to seizure induction. This series of events could still be provoked after destruction of the thalamus, except for the relay nucleus of the sensory pathway involved. It could be reproduced by direct stimulation of the thalamic sensory relay nuclei, but not the nuclei of the diffuse thalamic projection system. It was abolished by ablating the sensory receiving area of the cortex. The ascending sensory pathway and the cerebral cortex itself seem to be the only structures essentially involved in such seizure induction.

(Authors' abstr.)

Histochemical Studies of Active Carbonyl Groups (Proteolipids) in Brains with Multiple Sclerosis.

Twenty-two different brains from patients with multiple sclerosis were studied with a new reagent (2-hydroxy-3-naphtoic acid hydrazide coupled with tetrazotized diorthoanisidine) demonstrating the proteolipid (active carbonyl group) component.

The normal myelin as well as the remnants of myelin in the plaques were stained blue with this reagent. The areas of demyelination (plaques) stood out unstained. Also some gitter cells and macrophages showed blue granules (broken myelin). The ketonic carbonyl groups which were stained are probably identical with the proteolipid complexes isolated and crystalized from brain by Folch and Lees.

Destruction of the proteolipid fraction of the myelin sheath is a crucial element of the tissue damage in the lesions of multiple sclerosis. (Authors' abstr.)

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*Neuronographic Analysis of Medial and Basal Cerebral Cortex. I. Cat. II. Monkey. *MacLean, P. D., and Pribram, K. H.* . . . 312 and 324

Effects of Anterior Limbic Stimulation on Somato-motor and Electrocortical Activity.

1. The profound and immediate influences which—according to previous reports—the anterior limbic cortex can exert on the electrocorticogram (E.C.G.) and on movements induced by area 4 stimulation have been studied with simultaneous recordings of the electrical cortical activity and the motor responses in dialized cats and monkeys.

2. These studies indicate that anterior limbic stimulation can: (i) alter motor cortex induced movements in the direction of facilitation, inhibition, or facilitation reversing to inhibition, without any changes in the E.C.G., including that of the motor point in area 4; and (ii) induce widespread and profound E.C.G. changes, including that of the motor point in area 4, with or without simultaneous changes in the motor cortex induced movements—the most frequent combination, however, was that of the " attenuation " E.C.G. response with motor inhibition.

3. These responses were effected by means of subcortical projections from the anterior limbic cortex directly to subcortical levels of motor regulation and possibly also indirectly by cortico-subcortico-cortical paths to alter the excitability of the motor cortex.

4. Spread of electrical after-discharges from the stimulated anterior limbic cortex into the motor cortex has been demonstrated in cats with evidence of " secondary " facilitation followed by extinction at a cortical level.

5. The agranular anterior limbic cortex is therefore not accurately described as a " suppressor " area, but might perhaps better be termed " regulatory " in regard to its influence upon somato-motor activities.

6. Vocalization was obtained in the lightly anesthetized monkey from a small area restricted to the upper portion of the anterior limbic gyrus and to the banks of the cingulate sulcus.

7. Complex postural synergic movements of the limbs, trunk and neck, predominantly of contraversive type, were elicited in anesthetized cats and monkeys and in unanesthetized cats. These motor effects required a higher stimulus strength than that necessary for obtaining arrest of spontaneous movements, including respiration.

8. " Arrest " reactions with no loss in muscle tone have been elicited by anterior limbic stimulation in the unanesthetized cat. (Authors' abstr.)

Behavioral Changes Following Thalamic Injury in Cat.

Destruction of the thalamic mediodorsal nuclei in cats gives rise to behavioral changes, the outward manifestations of which can be described under the general headings of increased irritability and rage. In addition, such preparations display altered feeding habits, reduced motor activity, and decreased ability to solve problems in learning and discrimination. Conversely, destruction of the thalamic anterior nuclear complex is followed by an elevated threshold for the elicitation of rage, overly solicitous responses to pleasurable stimuli and docility. Combined injury of the thalamic anterior and mediodorsal nuclei occasions the development of labile behavior characterized principally by over-reactivity to both pleasurable and noxious stimuli. Finally, destruction of the thalamic intralaminar nuclei results in alterations of behavior characterized principally by transient lethargy, somnolence, motor disability and reduced reactivity to noxious stimuli.

(Authors' abstr.)

Independence of Diffuse Thalamo-cortical Projection System Shown by Specific Nuclear Destructions.

Cortical responses to local electrical stimulation of the diffuse thalamo-cortical projection system in cats under nembutal anesthesia have been recorded before and after selective destruction by coagulation of each of the specific thalamic nuclei, including lateral and medial geniculate bodies recording responses to visual and auditory cortex respectively, VPL to sensory cortex, VL to motor cortex, MD to frontal cortex, LP to parietal cortex, and the anterior nuclei to the anterior cingulate region.

The diffuse thalamo-cortical projection system may act independently of any of the specific nuclear projections to a given area of cortex. It does not necessarily reach the cortex via specific sensory or association nuclei, though it may provide intrathalamic interconnections between the latter as well.

Stimulation of a large bundle of fibres of the diffuse system in the ventral portion of VA may set up widespread short-latency responses, presumably due to stimulation of a large portion of the final common pathway of the diffuse projection system. More discrete stimuli set up local excitation which spreads by recruitment through a divergent multineuronal chain in the thalamus, producing cortical responses of much longer latency.

A topographical organization within the diffuse thalamo-cortical projection system (the thalamic reticular system) with projection to somato-sensory, visual, auditory, as well as to motor, frontal and parietal and cingulate cortex and to the caudate nucleus, has been confirmed. (Authors' abstr.)

An Experimental Study of the Transition from Normal to Convulsoid Cortical Activity.

The transition from normal to convulsoid activity was studied in 20 rabbits (minimal anesthesia). Paroxysms of slow development were initiated in the visual cortex by 11/sec. or slower repetitive stimuli to the geniculate. Leads which divided the cortex into several strata were used routinely to follow the development of paroxysm.

1. Prior to the appearance of paroxysm a progressive decline often occurred in amplitude of the responses to successive stimuli. This is called the low period. When the stimulus was broken during it, paroxysm usually developed slowly in the cortex.

2. Isolated clonic discharges, surface-positive in polarity, were the first overt evidence of paroxysm. These were followed by a period of fast tonic discharge which preceded build-up to the high-voltage paroxysmal pattern of the rodent. In rapidly developing paroxysm any or all of the above-mentioned phases can be missing.

3. Paroxysm occasioned by stimuli of quite slow frequency may demonstrate increasing prominence of the early negative phase (1) as a prelude to paroxysm. This relates the preparoxysmal status of the preparation to the sequence of events leading to the appearance of spontaneous strychnine spikes in other studies.

4. Most often paroxysm initiated in the cortex by repetitive thalamic stimulation was observed first in middle or superficial cortical fractions.

5. Paroxysms activated by intraperitoneal metrazol, or appearing spontaneously may also commence locally in the middle and superficial cortex as well as by developing simultaneously throughout. (Authors' abstr.)

Neuronographic Analysis of Medial and Basal Cerebral Cortex. I. Cat.

Phylogenetic, ontogenetic and cytoarchitectural studies, together with recent physiological and psychological investigations, suggest that the limbic system represents an early neural development involved in affectively determined processes. The limbic system comprises the cortex contained in the great limbic lobe of Broca and its associated subcortical cell stations. Further analysis of the functions of the limbic system requires a more detailed knowledge about its anatomical relationship with the rest of the nervous system. This investigation was undertaken to show on a comparative basis in the cat and the monkey the interrelationship of the limbic and extralimbic cortex. The method of physiological neuronography was employed for showing this relationship. This first paper reports the findings in the cat.

Eighteen animals were used in this study. The results indicate that five regions of limbic-extralimbic cortex can be differentiated if one allocates to a region all those areas of cortex that are reciprocally connected. Together these regions surround the hilus of the hemisphere. They are named according to their topographical location. Further analysis shows that the total area of cortex fired by all points within a region forms a large cortical segment. The five resulting segments collectively cover the entire cerebral mantle with the exception of parts of the visual, auditory and somatic areas.

In the subsequent paper it will be seen that limbic-extralimbic regions have been found in the monkey which, on a topographical basis, appear to be homologous to those described for the cat. It will also be seen that the large cortical segments associated with these regions follow a similar pattern in the monkey. The relevance of these regions and their associated segments to cortical function is at present being investigated and will be reported in subsequent communications.

(Authors' abstr.)

Neuronographic Analysis of Medial and Basal Cerebral Cortex. II. Monkey.

The method of strychnine neuronography has been used to explore the interconnections between the limbic and extralimbic cortex of the medial and basal aspects of the cerebral hemispheres. Large regional systems can be discerned on the basis of reciprocal connections of all points within such a region. Limits of the region are demarcated by lack of, or unidirectional, connections. The following regional systems have been described.

1. *Frontotemporal.*—The classification of this region is based on a firing pattern common to the strychninization of the posterior orbital, anterior insular, temporal polar and pyriform (periamygdaloid) areas. New findings include the demonstration of the firing pattern of the anterior insula as well as the reciprocal connections of the posterior orbital and insular cortex with the frontal operculum.
2. *Medial occipitotemporal.*—This region is characterized by the firing pattern common to the strychninization of the cortex of the hippocampal gyrus and portions of the fusiform and lingual gyri. New findings are two-way connections relating the limbic areas of the medial temporal cortex to a variable extent of medial occipital and medial temporal extralimbic cortex.
3. *Medial parieto-occipital.*—This region is delineated by the firing pattern common to the strychninization of the limbic cortex of the posterior cingulate and parasplenial gyri and the contiguous extralimbic cortex of the precuneus. Its connections with the hippocampus have been described.
4. *Medial frontoparietal.*—This regional classification is based on the firing pattern common to the strychninization of the rostral cingulate gyrus (limbic cortex) and the superior or frontal area (extralimbic cortex). The extent of firing of the medial cortex from the superior frontal area is surprising and has not been previously reported.
5. *Medial frontal.*—This region is delineated by the firing pattern common to the strychninization of the limbic cortex of the subcallosal and medial orbital areas, and the extralimbic cortex of the ventromedial frontal polar area. The demonstration of interconnections among these areas has not previously been reported.
6. *Hippocampus.*—Although no reciprocal connections between hippocampus and the other regions were established, the unidirectional firing of these regions into Ammon's formation is of interest. The anterior hippocampus is fired by the posterior orbital, anterior insular, and temporal polar and pyriform (periamygdaloid) areas. The posterior hippocampus is fired by the cortex of the hippocampal gyrus and the parasplenial and posterior cingulate areas.
7. The largest extent of cortex fired by strichninization of all points within a region is called a "segment." Cortical segments show considerable overlap at their borders.
8. Comparison of regions and segments in cat and monkey is made.
9. The methods for establishing the relevance of this classification of neuronographic data to problems of cortical function are referred to.

(Authors' abstr.)

JULY.

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Stimulation Studies of Insular Cortex of Macaca mulatta.

1. The effects of electrical stumulation of the insula on blood pressure, respiration, and stomach motility and tonus were studied in the monkey (*Macaca mulatta*). The following effects are produced : fall in blood pressure, inhibition of respiration in expiration, decrease in stomach tonus and inhibition of gastric peristalsis.
2. Similar effects were produced by stimulating the posterior orbital surface and the temporal pole, although the effects produced on blood pressure by stimulation of those areas were usually more variable than those produced by stimulation of the insula.
3. After sectioning both vagus nerves, the gastric responses no longer occurred, although the cardiovascular and respiratory responses persisted.
4. Electrical stimulation of the lateral surface of the cerebral hemisphere did not produce inhibition of respiration, fall in blood pressure or alterations of stomach tonus and motility, under the experimental conditions maintained throughout this study.
5. The typical responses to insular stimulation occurred regardless of the anesthetic agents used (dial, nembutal, ether or chloralosane-urethane).
6. Retrogasserian neurectomy, performed in two animals, did not abolish the gastric, respiratory or blood-pressure responses to stimulation of the insula.
7. The type of response obtained by electrical stimulation of the insula was not altered by varying the wave form, pulse duration or frequency of the stimulating current.
8. Square waves, sine, rectified sine and partially rectified sine waves were approximately equally effective in eliciting responses from the insula, but the exponentially falling type of wave required approximately twice the voltage of the other wave forms in order to produce the same affect.
9. Pulse durations of 3·0–10·0 m.sec. were found to be most effective, using the square wave form.
10. Frequencies of 20–100 pulses per sec. were found to be more effective than slower or faster frequencies, using the square wave form. (Authors' abstr.)

Spreading Cortical Convulsions and Depressions.

A transition of Leão's spreading depression into a convulsive pattern, moving at the same low velocity over the cortex, has been produced in a number of ways : (i) Repetition of stimulus eliciting the spreading depression causes spikes and high potential runs during the depression, which on further repetition may develop into a continuous convulsive pattern. (ii) An increase of the systemic blood pressure favors the development of convulsive patterns during the period of the spreading depression. (iii) An acute transition of the spreading depression into a spreading convulsive pattern is caused by the topical application of acetylcholine to the cortex, either in normal preparations or in preparations previously treated with prostigmin. (iv) The application of pilocarpine to the cortex had the same effect (v) Feeding 7–15 per cent. carbon dioxide into the apparatus for artificial respiration also causes the acute transition of a spreading depression into a spreading convulsive pattern. The slow potential change of the cortex, which invariably accompanies the spreading depression, was also found to accompany the spreading convulsive pattern.

These findings are discussed in their relation to previous observations which led to the conclusion that the spreading depression is accompanied by a wave of vasoconstriction. It was argued that the transition of the spreading depression into a spreading convulsive pattern is caused by interference with this wave of vasoconstriction, which was accomplished by exhausting the mechanism of vasoconstriction (repetition of the stimulus), by a marked increase of the blood pressure, or by the application of potent vasodilators (acetylcholine, pilocarpine, carbon dioxide).

Since neither adrenergic (yohimbine, ergotamine, dibenamine) nor cholinergic (atropine) blocking agents have been found to produce the acute transition from spreading depression into a spreading convulsive pattern, it was concluded that the mechanism of the postulated wave of vasoconstriction is neither adrenergic nor cholinergic in nature. (Authors' abstr.)

" Jump Reflex " in Hypothalamic Cat.

A jump reaction was observed in hypothalamic cats. The required conditions for provoking that response were analysed. Activation of deep proprioceptors of the neck and hind legs were found to be the principal receptors for the reflex. A particular order of neck and head movements is described as a " trigger " mechanism. Previous hypertonia of extensor muscles was required for the appearance of the phasic responses. Labyrinth and cutaneous receptors of the hind legs did not show participation in the reflex. Several stages of the jump reaction are described. The possible mechanism, integration of the reflex and facilitating influence of the hypothalamus are discussed. (Authors' abstr.)

Relation of Cerebellum to Upper Brain Stem.

Internal structures of the upper brain stem of the cat were systematically explored following electrical stimulation of various areas of the cerebellum.

Evoked potentials were especially prominent in two major systems of the brain stem, i.e., mesencephalic plus diencephalic tegmentum and many of the sensory relay nuclei of the thalamus. More variable responses were recorded from the mammillary bodies, hippocampus, globus pallidus, cerebral peduncle, superior colliculus and centromedial nucleus.

Latency of response ranged within three groups: (i) short, 1 m.sec. or less, categorized as asynaptic; (ii) medium, between 1 and 3 m.sec.; and (iii) long, over 3 m.sec. but usually below 12 m.sec.

Localized projections from anterior lobe, paramedian lobule, tuber vermis and ansiform lobule were observed, but our data were not conducive to detailed analysis of these projections.

The possible functional significance of a dual cerebellar projection, i.e., asynaptic and multisynaptic to related centers, is discussed as is a possible cerebellar rôle in the relay of various sensory modalities to the cerebrum. (Authors' abstr.)

Microelectrode Analysis of Pyramidal System During Transition from Sleep to Wakefulness.

1. A new preparation—the "pyramidal" cat—is described. This unanesthetized animal, which retains only the continuity of the cerebral peduncles following mesencephalic transection, exhibits spontaneously the characteristic E.E.G. and behavioral patterns of sleep.

2. Spike potentials have been recorded from the motor cortex of the cerebrum and from its efferent projections in the medulla oblongata through the use of fine wire microelectrodes.

3. The units examined were those which were spontaneously active only during the spindle waves recorded from the surface of the motor cortex. This activity, when present, was intimately correlated with each wave of the spindle complex.

4. Cortical activation, induced either by blowing unfiltered air into the nose or by electrical stimulation of appropriate regions of the thalamus, was paralleled by a complete blockade of the spike potentials. This abolition may be a result of the failure of ephaptic excitation or of an active inhibition of the neurons selected for study.

5. Local application of a dilute solution of strychnine (0·2 per cent.) to the motor cortex produced characteristic high frequency outbursts of activity in the intrinsic cerebral neurons and in the corresponding pyramidal tract. The convulsive dis-

charges and the corresponding strychnine waves were completely blocked for short intervals during olfactory or thalamic stimulation. The relation of this phenomenon to the mechanisms involved in the arousal reaction is discussed.

6. More concentrated solutions of strychnine (1 per cent.) augmented the frequency of the spike outbursts and the amplitude of the cortical wave. Stimuli previously effective in blocking the strychnine complex no longer produced a detectable change. (Authors' abstr.)

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Experimental Cerebral Concussion.

1. Acceleration concussion was studied in cats and monkeys with continuous recording of the electrical activity of cortex and certain brain stem structures, spinal fluid and blood pressures, and E.K.G. and respirations.

2. The electrical activity of the cortex was reduced in amplitude following concussion with little change in frequency and at times essentially no change was produced.

3. At no time was any massive epileptic-like discharge observed during the first few seconds after the blow. Such a process thus cannot be the mechanism of release of the acetylcholine that appears in the spinal fluid following concussion.

4. Changes in the electrical activity of brain stem structures largely paralleled those in the cortex except for the activity of the medial reticular formation where consistently greater depression of amplitude was seen as compared to cortex. The possible rôle of this phenomenon in the genesis of coma is discussed.

5. No change in spinal fluid pressure greater than 10 mm. of water was recorded during the first 5 hours following pure concussion. (Authors' abstr.)

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Effects of Inhibitors of Glutamine Synthesis on the Inhibition of Acetylcholine Synthesis in Brain Slices by Ammonium Ions. Braganca, Beatriz M., et al. [*Biochim. et Biophys. Acta*, **10**, 83 (1953).]

Substances which inhibit glutamine (I) synthesis produce a reduction of the inhibitory effect of NH_4 ions on the synthesis of acetylcholine (II) by rat brain slices. By using the technique of Mann *et al.* (*C. A.*, **33**, 8271^4) it was shown that inhibitors of (I) synthesis, such as methionine sulfoxide, ethionine sulfoxide, and methionine sulfoximine, decrease the inhibition by NH_4 ions of the rate of formation of bound (II); L-glutamate and DL-methionine do not have this effect. In respiring brain slices the presence of extra NH_4 ions increases the rate of formation of (I), diminishing the available adenosine triphosphate, and thus the rate at which (II) is synthesized. MORTON PADER (Chem. Abstr.).

Excitatory and Anticurare Properties of Acetylcholine and Related Quaternary Ammonium Compounds at the Neuro-muscular Junction. Riker, Walter F., jun. [*Pharmacol. Revs.*, **5**, 1–87.] L. E. GILSON (Chem. Abstr.).

Extraction of Acetylcholine from Brain Tissue. Crossland, J., and Merrick, A. J. [*Nature*, **171**, 267 (1953).]

The acetylcholine content of the brains of a series of adult rats, killed by immersion in liquid air, was 2·52γ/gm., while the excised brains of litter mates contained only 1·82γ/gm. For the determination of the absolute acetylcholine content of the brain the use of liquid air is the method of choice.

EDWARD J. VAN LOON (Chem. Abstr.).

Influence of Narcosis on the Amount of Acetylcholine Extractable from Motor Nerves. Kepka, Otto J. [*Z. Vitamin-, Hormon- u. Fermentforsch.*, **5**, 35 (1952) (*in German*).]

The plexus lumbosacralis and nervus ischiadicus of toads were used for these experiments. Reversible narcosis (use of saturated solution of ether for 10 minutes) caused no change in the amount of extractable acetylcholine ; irreversible narcosis in the presence of sufficient quantities of eserine to inhibit cholinesterase completely caused a decrease of one-third in the amount of extractable acetylcholine.

ERICH HIRSCHBERG (Chem. Abstr.).

Preparation of a Stable Brain Fraction Containing Acetylcholinesterase. Tauber, Henry. [*J. Am. Chem. Soc.*, **75**, 326–8 (1953).]

A rapid, convenient, and inexpensive method for the preparation of a stable fraction containing dry, soluble acetylcholinesterase (I) from frozen pig brain is described. Washed, frozen pig brain (450 gm.) was ground into a uniform paste with 150 gm. of sand and stirred for 5 minutes into 250 ml. of 0·05 M acetate buffer at pH 5·4 containing 1 ml. of Tween 21 and 15 ml. of toluene. After 24 hours at 37° the mixture was filtered, the filtrate was dialyzed 36 hours *vs.* 101 distilled H_2O containing 5 ml. of toluene, and then the dialyzed solution was treated with bentonite 0·8, $Ca_3(PO_4)_2$ 0·8, and hyflo 0·4 gm. per 100 ml. of solution. The clear yellow solution obtained after filtration or centrifugation upon lyophilization yielded 3 mgm. of enzyme preparation per ml. of filtrate. This (I) preparation hydrolyzed acetylcholine bromide 3 times faster than acetyl-β-methylcholine bromide and did not hydrolyze benzoylcholine chloride. This latter fact indicates the preparation is not contaminated with cholinesterase.

WALTER FRAJOLA (Chem. Abstr.).

Vitamin B_{12} and Acetylcholine Shock. Ogasawara, Kazuo, et al. [*Lancet*, **264**, 598 (1953).]

Mice injected intraperitoneally with 15γ vitamin B_{12} (I) 15–90 minutes before intravenous administration of 1 MLD histamine (II) all survived ; mice given (I) 2 hours before (II) were not protected from shock and death. Other mice were injected intraperitoneally with 15γ (I), and acetylcholine (III) (15 mgm./kgm.) was given 15 minutes later. All the animals died of shock. Mice injected intraperitoneally or intravenously with 15γ (I) at the same time as (III) recovered immediately from the slight signs of shock. However, the same amount of (I) simultaneously did not prevent shock when the dose of (III) was increased to 20 mgm./kgm. In rabbits (I) (in intravenous doses of 5–30γ/kgm.) did not modify the effect of (III) on the blood pressure.

BARBARA R. MURRAY (Chem. Abstr.).

Effect of Convulsion-inducing Agents on the Acetylcholine Content and on the Electrical Activity of the Brain. Torda, Clara. [*Am. J. Physiol.*, **173**, 179 (1953).]

During the preconvulsive phase the acetylcholine content of the brain increased from 10 to 150 per cent. after administration of physostigmine salicylate and to about 60 per cent. after administration of pentamethylenetetrazole. The acetylcholine content decreased about 30 per cent. after administration of NH_4Cl. Convulsions were initiated with NH_4Cl only when the acetylcholine content of the brain previously returned within normal limits. Convulsions do not occur with brain acetylcholine content below normal limits. The factor initiating convulsions may or may not be acetylcholine.

E. D. WALTER (Chem. Abstr.).

Effects of a Single Injection of Corticotropin (ACTH) on Ammonium Ion and Acetylcholine Content of the Brain. Torda, Clara. [*Am. J. Physiol.*, **173**, 176 (1953).]

Administration of corticotropin (ACTH) in a single injection induced in less than 30 seconds an increase of the NH_4 content of the brain. The NH_4 content returned to normal levels within 30 minutes and decreased by 30 per cent. within 1 hour. Administration of ACTH in a single injection induced an increase of the acetylcholine content of the brain in less than 30 seconds. Within a few minutes a peak value was reached, and the acetylcholine content returned to normal levels in less than 30 minutes. E. D. WALTER (Chem. Abstr.).

Acetylcholine Release in the Cat's Superior Cervical Ganglion. Perry, W. L. M. [*J. Physiol.*, **119**, 439 (1953).]

Acetylcholine (I) output from perfused eserinized cat's superior cervical ganglion falls approximately exponentially with time, under preganglionic stimulation, without any appreciable differences in total output for different frequencies of stimuli from 5 to 100/sec. Calculated initial (I) output per volley was about 10^{-11} gm. A second period of stimulation following an initial period yielded a very much reduced (I) output, unless the intervening rest was very long (35 minutes); this was not observed if the initial stimulation period was carried out in the absence of eserine (II) but the second period was carried out with (II). A non-stimulated perfused superior cervical ganglion yielded 100–400 $m\gamma$/minutes of choline (III) initially, falling rapidly after about 10 minutes to a steady level of from 20 to 60 $m\gamma$/minutes for different experiments. Stimulation increased this resting level of (III) by 20–50 $m\gamma$/minutes only for the first 5 minutes, after which no increase was observable in a perfused ganglion. These results confirm the tentative hypothesis that (I) liberated from the ganglion by a single preganglionic volley is a constant fraction of the "available" stock and that the synthesis of "available" (I) is a constant, independent of the rate of stimulation. On this hypothesis (II) acts to prevent hydrolysis and consequently resynthesis of liberated (I); this depletes the "available" stock of (I). In the absence of (II) this stock is little depleted and the amount of (I) liberated per volley remains practically constant.

MORRIS ROCKSTEIN (Chem. Abstr.).

The Role of Acetylcholine in Synaptic Transmission of Parasympathetic Ganglia. Perry, W. L. M., and Talesnik, J. [*J. Physiol.*, **119**, 455 (1953).]

By recording potential changes in response to retrograde injections through the cannulated lingual artery of decerebrate cats, 0·2 to 1 mgm. doses of acetylcholine (I) were observed to depolarize the cells of the ciliary ganglion, to block the ganglion action potential spike partially, and to alter the shape of the action potential resulting from submaximal preganglionic stimulation. 250γ doses of nicotine (II) produced changes similar to those of (I), which were also accompanied by constriction of the pupil. (II) had an effect on the pupil if the ciliary nerve had been severed. Hexamethonium (II) in 250γ doses produced a 30 per cent. block in spike height but without depolarization or change in shape characteristic of (I) and (II) block; it also had no blocking effects on postganglionic transmission to the pupil. Benzoylcholine in large doses (100γ to 3 mgm.) was inactive on the Langendorff preparation of the isolated cat heart when perfused through its coronary vessels. Fifty γ doses of (II) and 100γ doses of tetramethylammonium had the same inhibitory effect on the heart preparation as (I) or vagal stimulation. A large dose (6 mgm.) of (III) produced no direct effect but blocked inhibitory effects of small doses of (I) and (II) on the heart. In small doses (I) is inhibitory through stimulation of the intracardial vagal ganglion cells which can be blocked by (II) and (III); in larger doses its inhibitory effects are peripheral. These data support the hypothesis that transmission at the parasympathetic ganglion synapse is cholinergic. MORRIS ROCKSTEIN (Chem. Abstr.).

Effects of Close Arterial Injections of Acetylcholine on the Activity of the Cervical Spinal Cord of the Cat. Feldberg, W., et al. [*J. Physiol.*, **119**, 428 (1953).]

A special method is described for filling the vascular bed of a region being studied completely and quickly with drugs like acetylcholine (I). Injections of (I) (0·2 ml. of 10^{-4} solution) into the cervical spinal cord through the basilar artery caused an outburst of impulses lasting from 2 to 40 seconds in the first or second cervical nerve. (I) also increased the area of the ipsilateral polysynaptic reflex and decreased its latency ; close arterial injection of 80γ of atropine in 0·2 ml. failed to abolish the effect of (I). The changes in area were greater with supramaximal than with supramaximal stimuli. Injection of (I) increased the amplitude of the ventral root potential from ipsilateral stimulation and reduced the interval between stimulus and peak of the root potential by about 20 per cent. It also increased the variability of the level of the root potential at which the first impulse is excited. Eserine and prostigmine (0·2–0·5 ml. of a 10^{-4} solution) alone produced no effects on the untreated spinal cord and prolonged the effects of (I). Evidence from close arterial injections indicate that the predominant effect of (I) is the excitement of some interneurones, either by synaptic depolarization or by excitation of impulses at a nonsynaptic point which would facilitate the interneuronal synapse. MORRIS ROCKSTEIN (Chem. Abstr.).

Electrocorticographic Effects of Acetylcholine in Monkeys and Cats. Essig, Carl F., et al. [*Proc. Soc. Exptl. Biol. Med.*, **82**, 551 (1953).]

Tracings and discussion. L. E. GILSON (Chem. Abstr.).

Central Transmission by Afferent Impulses. II. Excitants, Acetylcholine, Adrenaline. Sterz, H. [*Naunyn-Schmiedeberg's Arch. exptl. Pathol. Pharmakol.*, **217**, 256 (1953).]

The spinal canal of decerebrate *Rana esculenta* was perfused from the upper end of the spinal column and the liquid collected from an opening at the lower end. The reactivity to electrical stimulation as modified by various chemicals was measured in one leg. Increased contractions were produced by strychnine at 1 : $10.^8$ The effect of picrotoxin HCl was similar but considerably weaker. Pervitin-HCl required a still higher concentration. These substances simultaneously augmented the number of reflex responses. Acetylcholine increased only the size, but not the frequency ; its effect was enhanced by eserine 9 to 10 times. Adrenaline was without effect. Histamine produced contraction without electrical stimulation and a generally increased tonus, and high concentration caused subsidence of the reflex responses. A. E. MEYER (Chem. Abstr.).

Experimental Production and Control of an Abnormality in Acetylcholine Metabolism Present in Epileptogenic Cortex. Tower, Donald B., and Elliott, K. A. C. [*J. Appl. Physiol.*, **5**, 375–91 (1953).]

A defect occurred in bound acetylcholine (I) metabolism in the cerebral cortex from animals with convulsions induced by methionine sulfoximine (II), and in normal cortical tissue when incubated under reduced O tension similar to that which occurred in slices of human focal epileptogenic cerebral cortex incubated *in vitro*. In all 3 conditions the free (I) production was normal during incubation. Treatment of animals with nembutal or avertin or the anticonvulsants dilantin or phenobarbital increased the production of bound (I) by excised cerebral cortex and overcame the depression of bound (I) in tissue from (II)-treated animals or that incubated under reduced O pressure. In contrast, tridione had no effect on the production of bound (I) under high or low O tension. Tridione and dilantin had no effect on (I) production *in vivo*, but phenobarbital reduced, by 50 per cent., the amount of free (I) synthesized at high K concentration. The convulsants, metrazole and picrotoxin, increased the (I) levels both *in vivo* and *in vitro*. The defect in the production of bound (I) in human epileptogenic cortex (III) was not found if the tissue was excised after the administration of general anaesthesia. The effect of the drug was not removed by rinsing the tissue. The presence of glutamine or asparagine, but not of glutamic acid, in the incubation medium restored to normal the production of bound (I) by (III), by cortex from (II)-treated animals, and by normal cortex incubated under reduced O tension ; half maximum effect was obtained with millimol of either substance. DL-glutamine, L-glutamine, and L-asparagine were equally effective at equimolar concentrations. When methionine was added to the medium, the defect was reversed in tissue from (II)-treated animals, but not in the other 2 cases. None of these substances had any effect on the (I) metabolism of fully oxygenated normal tissue.

THERESA MCKEE (Chem. Abstr.).

Microdetermination of Chlorides in Cerebrospinal Fluid (C.S.F.) and Other Organic Liquids. Gambardella, Alfonso. [*Ann. neurol.*, **58**, 193 (1952).]

Reagents : (A) dissolve 4 gm. Na tungstate in 1,000 c.c. H_2O and add 10 c.c. H_3PO_4 (d. = 1·72) ; (B) add KIO_3, 41·8 gm. in 1,000 c.c. H_2O to a solution of $AgNO_3$ (34 gm. in 1,000 c.c. H_2O), filter, wash, and store the precipitate ; (C) 0·2 gm. pyrogallol in 25 c.c. N H_2SO_4 and diluted to 100 c.c. Pour 2·5 c.c. (A) into a centrifuge tube, add 0·1 c.c. C.S.F., add 50 mg. (B) shake vigorously for 30 seconds and centrifuge. To 1 c.c. of the centrifuged liquid add 6 c.c. (C) and, within 5–20 minutes, read the light absorption with a colorimeter. Make standards with 0·1 N HCl.
C. Scandura (Chem. Abstr.).

Determination of Reducing Substances (Sugar) in Cerebrospinal Fluid (C.S.F.). Ragazzini, F. [*Riv. clin. pediat.*, **50**, 608 (1952).]

The following practical suggestions for a rapid (clinically adequate) analysis are given. Deproteinize C.S.F. by mixing 2·5 c.c. 0·9 per cent. $ZnSO_4.7H_2O$, 0·5 c.c. 0·2 N NaOH, and 2 c.c. C.S.F., and heat on a steam bath for 3–5 minutes. Add 0·15 c.c. A and B Fehling solutions to the filtered liquid (I), warm for 1·5–2 minutes, cool and (I) determine the reducing substances by nephelometry (standard curves made by the Hagedorn or Folin-Wu methods), or (II) filter and measure the residual blue color by a colorimeter. Another method : add 0·5 c.c. A and B Fehling solutions to 2·5 c.c. (I), centrifuge, decant, and measure the Cu_2O by dissolving it with 0·2 N H_2SO_4.
C. Scandura (Chem. Abstr.).

A Cadmium Sulfate Reaction on Cerebrospinal Fluid (C.S.F.). Brizzi, R. [*Riv. neurol.*, **20**, 179 (1950).]

The amount of 0·01 N HCl needed to dissolve the precipitate formed by mixing 1 c.c. of C.S.F. and 0·1 c.c. saturated solution. $CdSO_4$, was nearly 2·45 c.c. for normal subjects ; 2–2·25 in cases of progressive paralysis and meningeal reactions from hemorrhage ; 2·25–2·45 in some treated cases of progressive paralysis, in hydrocephalus and polysclerosis ; normal in affections of the peripheral nervous system, in some cases of tabes, in inflammatory processes and in a few cases of old progressive paralysis ; increased in a case of tuberculous meningitis and in cases of intracranial tumors.
C. Scandura (Chem. Abstr.).

The Passage of a Colloid from Cerebrospinal Fluid to Blood and Tissues. Howarth, F. [*Brit. J. Pharmacol.*, **7**, 573–80 (1952).]

A Pd^{109} colloid was prepared by the method of Paal and Amberger (Ber. **37**, 1, 124 (1904). Particle diams. were 54 per cent. 200 Å ; 15 per cent. 300 Å ; 15 per cent. 100 Å ; 11 per cent. 400 Å ; and 5 per cent. 500 Å in the supernatant after centrifugation 1 hour at 1,300 gm. After intravenous injection the rate of fall of the concentration of Pd in the blood depended partly on the size of the dose, large doses falling more slowly than small ones. After subarachnoid injection a small and variable concentration of Pd appeared in the blood. Tissue assay after injection by either route showed the lungs held a higher concentration than any other tissue examined except kidney, which after a subarachnoid dose showed a concentration comparable with that in lung. Richard F. Riley (Chem. Abstr.).

Sugar Content of Spinal Fluids. Nakane, Matsuyo. [*Igaku to Seibutsugaku* (*Med. and Biol.*), **10**, 246–8 (1947).]

Sugar content of spinal fluids (I), as determined by the $KMnO_4$ method of Shibata and N. (*C. A.*, **45**, 4768*e* ; **47**, 1218*f*), were expressed by : normal (I), $Z = 0·925 Z' + 0·0137$, and abnormal (I), $Z = 0·550 Z' + 0·0364$, Z and Z' were sugar contents (in gm./100 ml.) in Folin-Wu deproteinized filtrates and non-deproteinized filtrates, respectively. The difference $Z–Z'$ was independent of the sugar contents, and no statistically significant correlation was obtained between sugar and protein content of the fluids. The sugar contents of (I) decreased progressively with time on allowing the fluids to stand at room temperature. The decrease in deproteinized and non-deproteinized filtrates was expressed by : $Z = 1·00–0·07\ t$ and $Z' = 1·00–0·20\ t$, respectively in which initial sugar contents were taken as 1·00 t was days after sampling, and Z and Z' were sugar contents after standing, respectively.
M. Nakamura (Chem. Abstr.).

Practical Physiological Aspects of Cerebrospinal Fluid. Kalthoff, Robert J. [*Marquette Med. Rev.*, **13**, 124–31 (1947–48).]

Physiological, pathological and chemical aspects are reviewed. Twenty-three references. The physiological and clinical significance of serum phosphatase.
RICHARD R. BOLIN (Chem. Abstr.).

Practical Physiological Aspects of Cerebrospinal Fluid. Kalthoff, Robert J. [*Marquette Med. Rev.*, **13**, 146–51 (1947–48).]

A review on the physiological and pathological significance of alkaline and acid phosphatase. Eighteen references. W. C. TOBIE (Chem. Abstr.).

Content of Cells and Proteins in the Cerebrospinal Fluid. Neel, A. V. [*Nord. Med.*, **43**, 1022–25 (1950) (*in Danish*) ; *Excerpta Med.*, Sect. VIII, **4**, 19 (1951).]

A discussion.

The Rest Nitrogen Content of the Cerebrospinal Fluid. Pruckner, Franziska, et al. [*Arch. Psychiat. Nervenkrankh.*, **189**, 503 (1952).]

Total rest N (RN_2) and low molecular rest N (RN_1) were determined in cerebrospinal fluids from 51 normal subjects and from 351 patients with various diseases of the nervous system. The $RN_1 : RN_2$ ratio (NQ) varied from 1·3 to 1·7 in normals. NQ was in the normal range in most mental defectives, psychopaths and schizophrenics who had been shock treated, and below normal in most patients with meningitis, encephalitis, poliomyelitis, apoplexy and untreated schizophrenia. Normal and below normal NQs were about equally divided in multiple sclerotics and cerebral sclerotics. NQ was normal in 31 epileptics, definitely below normal in 8, and slightly below normal in 12. W. M. SPERRY (Chem. Abstr.).

The Nitrogen Quotient, a New Quantity for Characterizing the Cerebrospinal Fluid. Pruckner, F. [*Nervenarzt*, **24**, 30 (1953).]
WARREN M. SPERRY (Chem. Abstr.).

Sulfonamide Concentration in the Cerebrospinal Fluid during Inflammatory Reaction of the Fluid Space (Meninges) after Brain Operations. Driesen, Wilhelm. [*Deut. Z. Nervenheilk.*, **169**, 322 (1952).]

In 50 patients with aseptic meningitis after brain operations the sulfonamide (aristamide) (I) concentration was determined in blood and cerebrospinal fluid (C.S.F.). The cell count, total protein (II) concentration and Pandy and Nonne reactions (III) of C.S.F. were also determined. The ratio of concentrations of (I) in blood and C.S.F. ranged from 0·1 to 0·5, i.e., there was no increase in diffusion of (I) into the C.S.F. although in the majority of the C.S.F. (II) concentration and (III) were abnormal. WARREN M. SPERRY (Chem. Abstr.).

The Carbohydrate Content of Cerebrospinal Fluid Proteins. Stary, Z., et al. [*Klin. Wochschr.*, **31**, 339 (1953).]

Normal cerebrospinal fluid contains an average of 6·75 ± 2·45 mg. of protein-bound hexoses per l. ERICH HEFTMANN (Chem. Abstr.).

The Cerebrospinal Fluid. Talevalker, N. G. (*Antiseptic*, **50**, 161 (1953).]

A discussion. The importance of protein, chloride and urea contents of cerebrospinal fluid is reviewed. The use of Langes colloidal gold reaction as a diagnostic tool is described. THERESA MCKEE (Chem. Abstr.).

The Cause and Origin of Subacute Combined Degeneration of the Spinal Cord. Netousek, M. [*Neurol. Psychiat. Ceskoslovenska*, **11**, 157 (1948) ; *Excerpta Med.*, Sect. VIII, **2**, 746 (1949).]

A pathological and biochemical discussion. A lack of hematopoietic substance from the liver is only of secondary importance in producing spinal-cord degeneration in pernicious anemia. A lack of the B group of vitamins is more important.
W. C. TOBIE (Chem. Abstr.).

The Use of Radioisotopes for the Localization of Brain Tumors. Wrenn, Frank R., jun., and Good, Myron L. [*N. Carolina Med. J.*, **13**, 231 (1952).]

The technique of intracranial localization at the time of operation for brain tumor appears to be of limited value as an adjunct to standard neurosurgical procedure. The techniques for the pre-operative localization of brain tumors from without the intact skull have shown real promise of becoming an important diagnostic aid to the neurosurgeon. Of the latter techniques suggested to date, the use of I^{131} and diiodo^{131} fluorescein with the so-called normal method of counting appears to be most satisfactory. There is still need, however, for real improvement in the definition and accuracy of localization.

EDWARD J. VAN LOON (Chem. Abstr.).

The Influence of Female Endocrines on Epilepsy. Frohlich, Mayer. [*Intern. Record of Med.*, **166**, 9–11 (1953).]

Idiopathic epilepsy, if not occurring early in childhood, often appears at the age of puberty; in women, epileptiform seizures nearly always occur at a certain phase of the menstrual cycle, coincident with estrogen excess, either absolute or relative to progesterone deficiency, disturbing electrolyte and water metabolism.

J. DUFRENOY (Chem. Abstr.).

The Salt and Water Balance in Migraine. Campbell, Dorothy Adams, et al. [*Brit. Med. J.*, **11**, 1424–9 (1951).]

In the pre-migraine phase, and more particularly in the early stages of the attack, the blood Na concentration rose to a high level, while blood H_2O rose markedly. Excessive Na and Cl were excreted following inhibition of 1,500 ml. of H_2O.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Properties of Nerve Axons. I. Movement of Sodium and Potassium Ions during Nervous Activity. Hodgkin, A. L., and Huxley, A. F. [*Cold Spring Harbor Symposia Quant. Biol.*, **17**, 43 (1952).]

The mode is described in which cephalopod axons use the energy derived from the mixing of Na and K ions to generate and conduct an electric impulse. Tracer measurements show that the electric activity of cephalopod axons is associated with an inward movement of Na and an outward movement of K. Permeability changes underlying these ionic movements were studied by the voltage clamp technique. Depolarization leads to a rapid but transient increase in Na conductance and to a delayed but maintained increase in K conductance. Both effects are graded and can be reversed by repolarizing the membrane. Correct prediction of shape and velocity of the action potential and other related phenomena is possible by calculation.

HILDA H. WHEELER (Chem. Abstr.).

The Oxygen Uptake of Active Axons. Brink, Frank, jun., et al. [*Cold Spring Harbor Symposia Quant. Biol.*, **17**, 53 (1952).]

Characteristics of the chain of processes connecting impulse conduction in axons with O uptake from the environment were examined. Some of the phases discussed are: the kinetics of changes in O uptake by axons, the quantity of O per volley of impulses, properties of the time constants, utilization of the increased O metabolism associated with conduction of impulses, relation of the extra O uptake of active axons to that of a resting axon, and possible processes connecting conduction of impulses to rate of oxidation.

HILDA H. WHEELER (Chem. Abstr.).

Spinal Cord and Sympathetic Ganglia. Factors that Modify Transmission Through the Spinal Cord. Skoglund, C. R. [*Cold Spring Harbor Symposia Quant. Biol.*, **17**, 233 (1952).]

Differential actions of certain substances on different types of segmental reflexes were studied. Exposure to chemical agents was used to emphasize differences in the properties of various types of peripheral nerve fibers. In addition to studying the effect of chemical agents on transmission through mono- and multi-synaptic flexor and extensor systems, the effect on transmission through sensory synapses was investigated. The action of acetylcholine and anticholinesterases on spinal cord functions, and the action of adrenaline, noradrenaline and antiamine oxidases were recorded.

HILDA H. WHEELER (Chem. Abstr.).

Metabolic Requirements of Sympathetic Neurons. Larrabee, Martin G., and Bronk, Detlev W. [*Cold Spring Harbor Symposia Quant. Biol.*, **17**, 245 (1952).]

The principal points discussed are: (1) the measurement of rates of uptake of O and of glucose and changes in these rates produced by activity and by other modifications of metabolism; (2) the functional effects resulting from lack of O and of glucose, singly and in combination; and (3) the functional effects of other environmental changes which are believed to affect metabolism, including the effects of various metabolic poisons. HILDA H. WHEELER (Chem. Abstr.).

Histochemical Studies of the Glycogen of the Mammalian Brain. Shimizu, Nobuo, and Kumamoto, Tetsuzo. [*Anat. Record*, **114**, 479 (1952).]

Brain glycogen can be preserved when fixed by an adequate procedure, and can be demonstrated by the McManus method or lead tetraacetate method. The hypothalamus and area postrema are well supplied with glycogen.

EDWARD J. VAN LOON (Chem. Abstr.).

Glutamic Acid and Brain Tissue Respiration under Increased Oxygen Pressure. Gershenovich, Z. S., and Krichevskaya, A. A. [*Biokhimiya*, **17**, 684 (1952).]

The toxic effect of O under pressure is of importance in aviation. Glutamic acid, the only amino acid which is capable, like glucose, of maintaining brain-tissue respiration, has a protective effect on the organism during increased O pressure. The racemate was more effective than the L-form. Experiments were conducted on white rats and mice kept in a chamber for definite time intervals under an O pressure of 6 atmosphere. The brain was removed and the tissue respiration was measured manometrically. Increased O tension caused a decrease in tissue respiration, and this produced convulsions. The animals that had received 0·1 -1·0 gm. glutamic acid showed a higher tissue respiration, compared to the controls, and the convulsions started much later. Aspartic acid and alanine were entirely ineffective.

H. PRIESTLEY (Chem. Abstr.).

Functional Biochemistry of the Brain. Vladimirov, G. E. [*Fiziol. Zhur. S.S.S.R.*, **39**, 3 (1953).]

A review with new observations is presented. Introduction of camphor into mice increases lactic acid (I) in the brain owing to enhanced glycolysis, and the content of (I) is somewhat lower during pauses between spasms than during spasms. However, strychnine, which causes much stronger spasms and raises the blood level of (I) more significantly, does not cause a rise of brain (I) since (I) is transferred to the brain from the blood very slowly. Hence the rise of (I) in the brain is caused by actual alteration of carbohydrate metabolism in the brain proper. When the normal food supply to the brain is disturbed there is very rapid breakdown of phosphocreatine (II). Similarly, determination of adenosine triphosphate (ATP) in the brain after rapid freezing of the entire animal (rat) shows a much higher content than determined by previous investigators. Under physiological conditions of stimulation there is no decrease of ATP or (II) in the brain. The content of NH_3 found in the brain after quick freezing of an animal is some 0·1 of the values found after methods which allow for post-mortem changes in the tissue. NH_3 can be used as an index of the state of the brain: retarded or excited. Introduction of glutamic acid prior to introduction of NH_4 salts (unstated) serves to minimize or eliminate the toxic properties of the latter. Exchange of inorganic phosphates between blood plasma and brain tissue is very slow, and this transfer is controlled by the membranes which separate the circulatory system from the brain proper. The intracellular concentration of P is much higher than extracellular and if only the former value is taken into account it would explain the rapid restoration of ATP and (II) in the brain. The slowest P exchange is observed among the deoxyribonucleoproteins. The phosphoprotein fraction, which loses inorganic phosphate in N NaOH at 37° over 20 hours and which comprises some 4 mgm. per cent. of the tissue, shows unusually rapid P exchange, comparable to that of ATP and (II). These proteins show a greatly enhanced P exchange (or renewal) after stimulation of the brain tissue, which indicates that they participate in the act of transmission of the stimuli in the nervous-system tissues; an enhanced P exchange under these conditions also occurs in phospholipides and nucleoproteins.

G. M. KOSOLAPOFF (Chem. Abstr.).

Metabolic Changes in Coenzymes (I) and (II) by a System from Nervous Tissue. *McIlwain, H.* [*Intern. Congr. Biochem., Abstrs. of Commns. 1st Congr., Cambridge, Engl.*, 1949, 571.]

The process by which tissue preparations from the central nervous system liberate nicotinamide (I) from cozymase (II) proceeded at rates of 0·4–1·8 micromoles/mg. dry wt./hr.; this was often several times greater than the rate of respiration of the tissue. The reaction approached its maximum velocity at the normal, 5×10^{-4} M, concentration of (II) in brain tissue. (I), 10^{-3} M, reduced the breakdown of 3×10^{-4} M (II) by ½. The process resulted in the formation of one equivalent of acid per molecule (I) liberated. This was apparently caused by the disappearance of the pyridinium ion, and, when the reaction was carried out in $NaHCO_3$, its velocity could be followed manometrically by CO_2 evolution. The optimum pH was 7, and the reaction was almost unaffected by many inorganic salts. The system responsible for the reaction remained associated with tissue debris in isotonic solutions and was fairly stable at O or 37°, but was inactivated rapidly at 70°. It was easily obtained in H_2O solution and was purified. The same preparations also rapidly inactivated coenzyme II; the rate was 70-85 per cent. of that with (II). Inactivation of coenzyme II was also accompanied by the liberation of (I). Competition took place between the 2 coenzymes for the degrading system, thus a common enzyme was responsible in both cases. I derivatives, such as the ribofuranoside and glycosides, and dihydrocoenzyme I and II were not affected by the enzyme system. The system may participate in the control of E_H in equilibria of dehydrogenases, in aerobic phosphorylations, and in the route of carbohydrate metabolism. THERESA MCKEE (Chem. Abstr.).

Changes in the Nerve Membrane and the Role of Cholinesterase in the Conductive Process. *Bergmann, Felix, and Shimoni, Arela.* [*Biochem. et Biophys. Acta*, **10**, 49 (1953).]

Quaternary ammonium ions (I) inhibit the hydrolysis by acetylcholinesterase (II) of acetylcholine and of neutral esters. The inhibition is competitive. The relation of (I) to the active surface of (II) parallels the behavior of (I) to cation-exchange resins. Therefore, when the enzyme is built into the nerve membrane the membrane acquires the properties of a "permselective" membrane. The conductive process in the nerve membrane may be explained as follows: When the action current flows across the membrane, in the first line a shift of H ions occurs owing to the high mobility of H^+. The concentration and activity of H^+ in the hydrated parts of the membrane are thus changed. Simultaneously, the H-bonded network and selective permeability of the membrane break down. The recovery process is dependent on a chemical change in the membrane itself.

MORTON PADER (Chem. Abstr.).

The Metabolism of Various Brain Tissue Preparations. *Elliott, K. A. C., et. al* [*Intern. Congr. Biochem., Abstrs. of Commns., 1st Congr., Cambridge, Engl.*, 1949, 603.]

The pretreatment of brain-cortex slices affects aspects of their metabolism. If slices are kept in a glucose-containing medium, aerobic glycolysis occurs actively for a short time, then falls to a low value. Slices which are stored in a humid chamber without moistening, or kept in a glucose-free medium for 30 minutes, show a high and sustained aerobic glycolysis. The respiration of the humid-stored slices is as high as that of the other slices, but they are less stimulated on the addition of 0·1 M KCl to the medium. Homogenous brain suspensions prepared in isotonic media respire or carry on anaerobic glycolysis at 70 per cent. of the rate of slices of the same tissue. The optimum pH for respiration of the suspensions is 7·0–7·5, whereas with slices maximum respiration occurs at pH 9·5. The anaerobic glycolysis of the slices has an optimum at pH 7·0; the addition of pyruvate stimulates the rate and causes it to be maintained at a higher pH. The aerobic glycolysis of the suspensions is lower than that of slices; it increases with pH, and at pH 6·5 acid formation ceases or becomes negative. Bicarbonate or CO_2 does not simulate brain tissue metabolism and slightly inhibits respiration and glycolysis. Water homogenates of brain tissue metabolize at a low rate until various co-factors are added. The metabolism of isotonic suspensions approaches that of slices and respiration and pyruvate-stimulated anaerobic glycolysis are not affected by nicotinamide, diphosphopyridine nucleotide or phosphocreatine. Apparently even though the cells are largely disrupted, essential coenzymes are maintained in an active form in which they are not readily subject to attack by destructive enzymes.

THERESA MCKEE (Chem. Abstr.).

Acid-soluble Phosphates in Monkey Brain as Affected by Certain Central Nervous System Stimulants and Depressants. Shideman, F. E., and Seevers, M. H. [*Proc. Soc. Exptl. Biol. Med.*, **82**, 63 (1953).]

The influence of d-tubocurarine, pentobarbital, chloral hydrate, pentylenetetrazole, and 5-ethyl-5-(1, 3-dimethylbutyl) barbituric acid on the concentrations of inorganic phosphate, phosphocreatine, and adenosine triphosphate in the cerebrum of the *rhesus* monkey was studied. d-Tubocurarine was the only one producing a significant effect; it decreased the phosphocreatine only.

L. E. GILSON (Chem. Abstr.).

Pseudocholinesterase of Brain. Mendel, B., and Myers, D. K. [*Nature*, **170**, 928 (1952).]

Administration of tri-o-tolyl phosphate (I) which is known to be a selective inhibitor of pseudocholinesterase (II) to rats, produced a complete inhibition of (II) in the brain. Histological examination of the brain, spinal cord and sciatic nerves of these animals did not reveal any demyelination or other abnormalities. It is concluded that the activity of (II) has no relation to the integrity of the medullated nerve fiber, and secondly that (II) is not required for the hydrolysis of acetylcholine released by the nervous activity of the brain.

L. WEIL (Chem. Abstr.).

Cerebral Cholinesterase in Experimental Anaphylactic Shock in Guinea-pigs. Poloni, Alfredo. [*Riv. neurol.*, **20**, 251 (1950).]

The cholinesterase activity of the cerebellar cortex of guinea-pigs examined 0·5 hour after death, during the shock, and 2 hours after initiation of shock with and without severe convulsions was, respectively, 67·48, 40 and 12·42 per cent. higher than in controls. C. SCANDURA (Chem. Abstr.).

The Cadmium Reaction in Nervous and Mental Diseases. Benassi, P. [*Riv. neurol.*, **20**, 515 (1950).]

The reaction of Wunderly and Wuhrmann was applied to 555 cases of nervous and mental diseases: no significant positive results were obtained.

C. SCANDURA (Chem. Abstr.).

Phenylpyruvic Oligophrenia. Phenylpyruvic Acid Content of Blood. Jervis, Geo. A. [*Proc. Soc. Exptl. Biol. Med.*, **81**, 715 (1952).]

The method for the determination of blood phenylpyruvic acid is given in detail. Normal persons gave values of 0·014 mgm. per cent., whereas persons affected with phenylpyruvic oligophrenia gave values ranging from 0·31 to 1·78 mgm. per cent. A significant increase in phenylketonemia was observed following ingestion of DL-phenylalanine, the D form causing a considerably greater increase than the L isomer. Feeding of phenylpyruvic acid resulted in a sharp increase of phenylketonemia. EDWARD J. VAN LOON (Chem. Abstr.).

Measurements of Adrenal Cortical Activity in Young Men Subjected to Acute Stress. Kuhl, W. James, jun., et al. [*J. Clin. Endocrinol. and Metabolism*, **12**, 393 (1952).]

Norman subjects were immersed in water at 9·5° for 8 minutes. Changes occurring in the blood immediately or within 4 hours were increases in neutrophils, serum proteins, and free and esterified cholesterol; and decreases in lymphocytes, eosinophils, NaCl, and serum water. The urine showed increases in Na, ascorbic acid and the uric acid/creatinine ratio. Some of these changes are indicative of increased adrenal cortical activity. Serum Na, plasma K, blood sugar, blood ascorbic acid, and urinary K and Cl showed no significant changes.

L. E. GILSON (Chem. Abstr.).

Histochemical Localization of Acetylcholinesterase in Nervous Tissue. Ravin, Herbert A., et al. [*J. Pharmacol. Exptl. Therap.*, **107**, 37 (1953).]

A new method based on the acetylesterase function of acetylcholinesterase in fresh frozen tissue was developed. 2-Naphthalene acetate was used as the substrate in conjunction with the dye Fast Blue R.R. Enzymic activity was demonstrated in the cytoplasm and cell membrane of neurocytes. in the neuropile and in myoneural junctions. Cell nuclei were free of enzymic activity.

J. D. Taylor (Chem. Abstr.).

Quantitative Changes of Nucleotides in the Diencephalon, Liver, Kidney and Adrenal Glands of White Rats Treated by Electroshock. Gherarducci, Domenico. [*Sistema nervoso*, **3**, 411 (1951).]

Histological observations showed that only one electric stimulation caused slight changes in the ribonucleic acid (I) content of the cells of the above organs ; repeated stimulations within 2 hours 6 days caused an increase of the cell function (decrease of (I)) with protein and nucleotide disintegration following and therefore protein and nucleotide decrease. The changes were irreversible only in cases of repeated treatments within a few hours. No changes were observed in the deoxyribonucleic acid.

C. Scandura (Chem. Abstr.).

Lead Poisoning as a Cause of the Athetoid Type of Cerebral Palsy. Martin, Robert V., and Shapiro, Allen D. [*Arch. Pediat.*, **70**, 20 (1953).]

This type of cerebral palsy occurred in a 5-year-old child suffering from chronic Pb poisoning. The urine (700 c.c.) contained 0·035 mgm. Pb (0·05 mgm./1) and a trace of albumin. X-ray examination revealed lead lines at the knees, wrists and iliac crest, and the deep bands of increased *d* characteristic of Pb poisoning at the angles of the scapulae and in the sternal ends of the ribs.

Joseph S. Hepburn (Chem. Abstr.).

Residual Neuropathological Effects of Cyanide Poisoning. A Study of the Central Nervous Sytsem of Twenty-three Dogs Exposed to Cyanide Compounds. Haymaker, Webb, et al. [*Military Surgeon*, **3**, 231–46 (1952).]

Dogs were exposed in a single exposure to CNCl and HCN by inhalation and NaCN and CNCl by intravenous injection. In 7 dogs which died within 3 hours, no significant changes were found in the central nervous system. In 15 dogs, gray matter suffered heavily (total necrosis) and almost exclusively. The structures most susceptible in approximate order of decreasing frequency of involvement were cerebral cortex, head of the caudate nucleus, putamen, substantia nigra, globus pallidus, pulvinar of the thalamus, and cerebellar cortex.

J. D. Taylor (Chem. Abstr.).

Motor End-plate Difference as a Determining Factor in the Mode of Action of Neuromuscular Blocking Substances. Zaimis, Eleanor J. [*Nature*, **170**, 617 (1952).]

Decamethonium (I) and succinylcholine, neuromuscular blocking agents, produced blocking effects in monkeys, dogs and hares which were at first characteristic of depolarization at the end-plate followed by a transition to a competitive inhibitor type of block. In the cat and human (I) acts only by depolarization. Tridecamethonium, a higher member of the methonium series, showed the same type of blocking action in the cat as did (I) in the dog and monkey.

Gordon W. Newell (Chem. Abstr.).

Motor End-plate Differences as a Determining Factor in the Mode of Action of Neuromuscular Blocking Substances. Churchill-Davidson, H. C., and Richardson, A. T. [*Nature*, **170**, 617–18 (1952).]

Decamethonium (I) produces a neuromuscular block typical of competitive inhibition in patients with myasthenia gravis as contrasted with a depolarizing block obtained with the same compound in normal patients. (I) is excreted at the same rate and unchanged in both types of subjects. The condition of myasthenia gravis may cause acetylcholine to function as a competitive inhibitor in neuromuscular transmission at the motor end-plates.

Gordon W. Newell (Chem. Abstr.).

The Role of Enzymes in Alcohol Metabolism. Lecoq, Raoul. [*Presse méd.*, **60**, 1662–4 (1952).]

The toxic effect of EtOH is caused by the following metabolites: MeCHO, $MeCOCO_2H$, and "CPF," a derivement of $MeCOCO_2H$, that potentiates the effect of the acid. The most important enzymes involved in the metabolism of EtOH are dehydrases with codehydrases, the latter derived from the nicotinamide-adenine complex. H transmitters like glutathione also are of influence. The potential enzyme mechanism in the liver is discussed. Undernutrition and hormonal unbalance impair alcohol metabolism. A. E. MEYER (Chem. Abstr.).

Judgment of Fresh Brain Concussion by the Fasting Blood Sugar and Simultaneous Osmotherapy with Levulose. Moser, Herbert. [*Arztl. Monatsh.*, **5**, 827–33 (1949–52).]

Severity, healing, and prognosis of concussion were investigated in 552 cases by determination of the fasting blood-sugar curve without tolerance test. Intravenous injections of 20 c.c. 40 per cent. levulose combine the advantage of treatment with diagnosis. Patients under the influence of EtOH awake rapidly with levulose because of transformation of the sugar into $MeCOCO_2H$; unconsciousness due to concussion does not yield to levulose. A. E. MEYER (Chem. Abstr.).

Morphological Alterations in the Brain after Intoxication with Parathion. Siedek, H., and Thaler, H. [*Arch. intern. pharmacodynamie*, **91**, 194–201 (1952).]

Dogs were repeatedly poisoned with parathion and treated with atropine, so that up to 98 mgm./kgm. was given over a period of 22 days. Animals which died had severe hyperemia of the brain and spinal cord. Degeneration of the ganglionic cells is present after 30 hours, and of the myelin sheaths in experiments of long duration. M. L. C. B. (Chem. Abstr.).

The Metabolic Disorder in Hepato-lenticular Degeneration. Matthews, W. B., et al. [*Quart. J. Med.*, **21**, 425–46 (1952).]

Two cases of hepato-lenticular degeneration are described, together with the results of investigations of the metabolism and excretion of amino acids and Cu. Excessive urinary excretion of amino acids was caused by a tubular defect, as shown by determinations of serum and urinary amino N, by paper chromatography, and by determinations of amino N clearances after ingestion of glycine and alanine. Both patients had an abnormally high urinary excretion of Cu, which was further increased by injection of BAL or of a complex organic Cu compound "cuprelone," but similar changes were produced in normal subjects. However there is a specific abnormality of Cu metabolism in acromegaly. It is postulated that there is both an increased tissue reserve of Cu, and a renal defect as regards Cu as well as amino acids. JOHN T. MYERS (Chem. Abstr.).

Comparative Study of the Biochemical Development of the Brain of Some Species of Mammals. Mandel, Paul, and Bieth, Robert. [*Compt. rend.*, **235**, 485–7 (1952).]

Deoxypentose nucleic acid (DNA) is an essential constituent of chromosomes. Therefore the amount of DNA in the brain is related directly to the multiplication of cell nuclei. When DNA reaches a maximum level it is assumed that the number of cells in the brain also arrives at a maximum value. Since the guinea-pig at one day of age has the same amount of DNA in the brain as an adult, it is concluded that the cellular growth of the brain is terminated at birth. In the rat, cellular growth stops after 16 days, in the rabbit and the cat after 1 month, and in the dog after 5 months. With the human it has not been possible to fix the exact time, but according to available data, cellular multiplication ceases at approximately 1 year of age. Other brain constituents, such as proteins, lipides, and especially phosphatides, continue to increase for a variable period of time depending on the species. The amount of pentose nucleic acid (PNA) reaches a maximum at the same time as DNA in the rat, rabbit and the cat, but at a later time in the guinea-pig. In man, at the moment when the increase in the number of cells is terminated, apparently the amount of PNA is much less than that found in the adult brain.
N. R. STEPHENSON (Chem. Abstr.).

Respiratory Activity of the Cerebral Cortex in vitro *in Relation to the Concentration of Glucose in the Medium. Maleci, O.* [*Boll. soc. ital. biol. sper.*, **23**, 58–61 (1947); *Excerpta Med.*, Sect. II, **1**, 340 (1948).]

The respiration of rabbit cerebral cortex was measured in a Warburg apparatus in Ringer solution containing various concentrations of glucose. Respiration increased up to a maximum of 0·04 per cent. glucose; higher concentrations caused no increase in respiratory activity. The normal concentration of glucose in cerebrospinal fluid is 0·05–0·06 per cent. W. C. TOBIE (Chem. Abstr.).

The Chemical Origin of Electrical Energy in the Nervous System. Barnes, T. Cunliffe. (*Euclides*, **10**, 118–21 (1950).]

The theory that explains the electrical nerve impulse as a diffusion potential is shown to be untenable on experimental and theoretical grounds. The electrogenic action of acetylcholine and other quadricovalent N compounds can be demonstrated *in vitro* and *in vivo*. The spike produced by an onium salt on non-medullated nerve of *Homarus americanus* is described. It is concluded that the basis of nervous energy resides in the phase-boundary electrical potential generated by compounds in the nervous system containing quadricovalent N.

ELVA G. SHIPLEY (Chem. Abstr.).

The Glycemic Curve after Prefrontal Leukotomy. Pirovano, A., and Confortini, C. [*Minervachir*, **7**, 397–400 (1952).]

In 5 dogs subjected to bilateral leukotomy the glucose content of blood increased from 0·08–0·1 to 0·18–0·2 per cent. 30 minutes after the operation. The initial values were restored within 2 hours. These facts are discussed.

C. SCANDURA (Chem. Abstr.).

Magnesium Molybdate in Psychic Anorexia. Caujolle, F., et al. [*Toulouse med.*, **53**, 341–52 (1952).]

A review on the metabolic effect on Mo and clinical cases.

GEO. SAG (Chem. Abstr.).

Effect of Tetraethyl Lead Poisoning on the Higher Nervous Activity of Animals (*White Rats*). *Gorsheleve, L. S.* [*Zhur. Vysshei̮ Nervnoi̮ Deyatel'nosti im. I. P. Pavlova*, **1**, 727–38 (1951).]

Subcutaneous introduction of 0·04 gm./kgm. of Et_4Pb into rats leads to a three-phase serious alteration of activity of the higher nervous system. In the first phase the cortical activity and stimulability are increased with decrease of latent period of conditioned reflexes. In the second phase the blocking process mounts and its course spreads to subcortical layers leading to chaotic motor functions. The last, third, phase is that of restoration of functions, first the unconditioned, then the conditioned reflexes being normalized. Generally animals with weak level of nervous activity suffer more severe symptoms of such intoxication than do animals with a high level of nervous activity, or animals of nervously stable type.

G. M. KOSOLAPOFF (Chem. Abstr.).

Influence of Deoxycorticosterone on Potassium Concentration in the Serum and in the Cerebrospinal Fluid. Bekaert, J., and Demeester, G. [*Arch. intern. physiol.*, **59**, 391–2 (1951) (*in English*).]

Dog cerebrospinal fluid, taken by suboccipital puncture, and arterial blood were examined for K after daily injections of 5–10 mgm. deoxycorticosterone/kgm. for 3–8 days. Spinal fluid K decreased slightly while the serum level dropped from control values of 19–22 to 11–16 mgm. per cent. C. D. J. (Chem. Abstr.).

Influence of the Infusion of Potassium Chloride on the Cerebrospinal Fluid Concentration of Potassium. [*Arch. intern. physiol.*, **59**, 393–4 (1951); *C. A.*, **47**, 2860*e*.]

The intravenous infusion of 150–800 ml. of isotonic KCl into dogs over 2–3 hours' time produced marked increases in serum K, while the spinal fluid K did not change. Within 10–20 minutes after death the K content of the spinal fluid increased from 11 to 19–25 mgm. per cent., however. C. D. J. (Chem. Abstr.).

Ammonium Ion Content and Electrical Activity of the Brain during the Preconvulsive and Convulsive Phases Induced by Various Convulsants. Torda, Clara. [*J. Pharmacol. Exptl. Therap.*, **107**, 197–203 (1953).

In rats the brain NH_4 ion content (I) remained within normal limits during the preconvulsive phase induced by physostigmine salicylate and pentylenetetrazole and increased up to 9-fold during the preconvulsive phase induced by NH_4Cl. Convulsions were induced by NH_4Cl only when the (I) exceeded 10 times the control values. (I) increased during convulsions induced by various agents. The changes in the electrical activity of the brain during the preconvulsive and convulsive phases are described. It appears that an accumulation of NH_4 ion in the brain is the result of increased cerebral activity and is not necessarily the factor initiating convulsions. One of the physiological effects of the accumulation of NH_4+ is to contribute to the termination of convulsions. L. E. GILSON (Chem. Abstr.).

The Quick Test in Schizophrenia. Pieper, Josef, and Faber, Rolf. [*Klin. Wochschr.*, **31**, 157–8 (1953).]

Schizophrenic and other mental patients showed a diminished hippuric acid excretion in the Quick test. This is believed due to a glycine deficiency, but not to an accumulation of some toxic material. E. HEFTMANN (Chem. Abstr.).

Aging of Neurofibrils. Sosa, Julio María. [*J. Gerontol.*, **7**, 191–5 (1952).]

A special change of the neurofibrils network occurring in relation to the accumulation of lipochrome pigment (lipofuscin) in the cytoplasm is described and is designated as lipochrome neurofibrillar degeneration or lipofuscin neurofibrillar degeneration. The degeneration begins with a dissociation and agglutination of the neurofibrils and ends with total neurofibrillolysis. Three distinct stages of the degenerative process are described. It is considered that the process is one of aging. THERESA McKEE (Chem. Abstr.).

Biochemical Evolution of the Brain in Ontogenesis and Nervous Activity. Kreps, E. M., et al. [*Zhur. Vyssheĭ Nervnoĭ Deyatel'nosti im. I. P. Pavlova*, **2**, 46–57 (1952).]

A review with experiments conducted on rabbit, guinea-pig, hen and grackle at various ages. These experiments indicate that the development of the enzyme systems of the cerebral cortex, the maturation of cell structures, and the maturation of bioelectrical activity are correlated to the development of chemical, structural and functional characteristics. The cortex matures at a later date than do the other parts of the brain, and the level of enzymic activity in the cortex is also higher than that found in other brain tissues.

G. M. KOSOLAPOFF (Chem. Abstr.).

Content of Readily Hydrolyzable Compounds Containing Hexosamine in Human Brain. Kuzin, A. M., and Garzunova, G. A. [*Doklady Akad. Nauk S.S.S.R.*, **87**, 833–35 (1952).]

In an examination of 23 individuals it was determined that the grey matter of the brain contains more hexosamine (450–650 mgm. per cent.) than does the white matter (290–417); the temple regions have the highest level (633) and the back of the head and the forehead regions have the lowest (500–433).

G. M. KOSOLAPOFF (Chem. Abstr.).

Distribution of Bromides in Various Parts of the Central Nervous System of Dogs and Rabbits as Studied with the Aid of Bromine Radioisotope (Br^{82}). *Verkhovskaya, I. N.* [*Doklady Akad. Nauk S.S.S.R.*, **87**, 681–4 (1952).]

Subcutaneous introduction of $NaBr^{82}$ (60–70 μc. per kgm.) in presence of carrier NaBr (20–40 mgm.) gave results which are shown on bar graphs. In the dog the Br^{82} concentration in the brain tissue is very low (17–22 per cent.), while the blood supply to the brain has 100 per cent. activity and the spinal fluid has 62 per cent. activity. Hypothalamus has 27 per cent. activity, and hypophysis 32 per cent. Gastric mucous membrane has 102 per cent. activity, outer layers of the kidney 90 per cent., urine 72 per cent., liver 56 per cent., thyroid 50 per cent.; in descending order follow lungs, kidney cortex, adrenals, and spleen; the least activity (18 per cent.) was found in the muscle. In rabbits very little activity is found in the brain tissue, although up to 45 per cent. is found in the hypothalamus and 50-60 per cent. in the hypophysis. Thyroid had nearly 100 per cent. activity, while muscle tissue had under 20 per cent. G. M. KOSOLAPOFF (Chem. Abstr.).

Staining of Nerve Fibers with Methylene Blue. Factors Improving the Staining. Nelemans, F. A., and Dogteron, J. [*Stain Technol.*, **28**, 81–5 (1953).]

Important factors in immersion staining of the intestine are: (I) methylene blue solutions, free of Zn, that can be kept for weeks and months at 37°; (2) temperature 15–21° (for mammals); (3) pH about 6·9; (4) isotonic or slightly hypnotic solutions; (5) solutions kept saturated with O (of air); (6) high tonus of the vagus nerve by chloral hydrate as anesthetic and carbaminoylcholine in the staining solution; (7) anesthetics (alcohol urethan, chloral hydrate) added to the staining solution presumably lessening the vitality of the nervous tissue. For other organs, modify the concentration of the anesthetic added to the staining solution and the pH. W. B. ESSELEN (Chem. Abstr.).

Physiopathological Features of Cortical Oxygen. Rémond, A. [*Rev. neurol.*, **80**, 579–88 (1948); *Abstracts World Med.*, **6**, 267 (1949).]

Quantitative determinations were made of (O) tension in different parts of exposed cortex in cats under nembutal anesthesia. Diffusion of (O) into the cortical tissue occurred on the venous side. During nikethamide convulsions the (O) tension diminished in the venous blood draining from a cortical area, probably as a result of increased utilization of (O) in the cortex during the seizure.
W. C. TOBIE (Chem. Abstr.).

Phenylpyruvic Oligophrenia Deficiency of the Phenylalanine Oxidizing System. Jarvis, Geo. A. [*Proc. Soc. Exptl. Biol. Med.*, **82**, 514–15 (1953).]

Extracts of livers of 2 phenylketonuric patients failed to catalyze the conversion of phenylalanine to tyrosine in the presence of (O_2), phosphopyridine nucleotide and nicotinamide. Similar extracts of livers from patients dying of other diseases readily effected the conversion. L. E. GILSON (Chem. Abstr.).

Periodic Functional Changes in the Hypothalamus as Related to the Gonad Cycle. Gitsch, E. [*Arch. Gynäkol.*, **182**, 52–7 (1952).]

The acetylcholine content of the central hypothalamus was measured in 92 albino rats. During proestrus the total acetylcholine content is 4·24 ± 0·427 γ/gm., during estrus 3·99 ± 0·458 γ/gm., during metestrus 2·21 ± 0·08 γ/gm. During anestrus 1·32 ± 0·071 γ/gm., and during the proestrus-estrus stage 4·41 ± 0·263 γ/gm. The variations in the acetylcholine content of the frontal lobes is not as distinct as in the hypothalamus. DORIT L. NOETHER (Chem. Abstr.).

Pregnancy and Hypothalamus. Gitsch, E. [*Arch. Gynäkol.*, **182**, 58–60 (1952).]

The total acetylcholine content of the hypothalamus and the frontal lobes in pregnant albino rats was measured on the 6th, 13th and 20th day of pregnancy. The hypothalamus contains 1·48 ± 0·106 γ/gm., 2·07 ± 0·21 γ/gm., and 3·76 ± 0·32 γ/gm., respectively, while the values for the frontal lobes are 1·404 ± 0·18, 1·56 ± 0·206, and 2·25 ± 0·28 γ/gm. DORIT L. NOETHER (Chem. Abstr.).

Isolation from Mammalian Brain of Coproporphyrin III and a Uro-type Porphyrin. Blanshard, T. Paul. [*Proc. Soc. Exptl. Biol. Med.*, **82**, 512–13 (1953).]

The isolation from beef brain of crystallized coproporphyrin III and of an unidentified uro-type porphyrin is described. The Me ester of the latter m. 273–4°, significantly lower than uroporphyrin (I) Me ester. The Soret absorption band also differed. L. E. GILSON (Chem. Abstr.).

Changes in the Cholinesterase Activity (of Blood) after Infiltration of Ganglionectomy of the Lumbar Sympathetic. Del Bello, P., and Venturini, A. [*Arch. ital. chir.*, **74**, 313 (1951).]

The cholinesterase activity of blood did not change after infiltration of the lumbar sympathetic with alcohol-procaine (10 cases), but increased in 3 of 9 cases after ganglionectomy. C. SCANDURA (Chem. Abstr.).

Neurological Hepatic Symptoms in Wilson's Disease. Amyot, R. [*Union med. Canada*, **79**, 372–80 (1950); *Excerpta Med.*, Sect. VIII, **4**, 26 (1951).]

Of 4 cases, 3 showed pathological liver function tests (cephalin, bromosulfalein, hippuric acid), hyperglycemia and glycosuria, 2 of which also showed urobilinuria, hypoprothrombinemia and a positive galactose test.

W. C. TOBIE (Chem. Abstr.).

Vegetative Regulatory Activity in Postencephalitic Conditions. Sturm, A. (*Stadtischen Krankenanstalten, Wuppertal-Barman, Ger.*). [*Med. Klin.* (*Berlin*), **44**, 33–7 (1949); *Excerpta Med.*, Sect. VIII, **3**, 348 (1950).]

The applications of chemical tests (adrenaline, insulin, glucose tolerance, etc.) in the diagnosis of diencephalic vegetative regulation are discussed in relation to pathological changes. W. C. TOBIE (Chem. Abstr.).

Lactic Acid Response to Muscular Exercise in Neurocirculatory Asthenia. Linko, Eino. [*Ann. med. intern. Fenniae*, **39**, 161 (1950).]

Lactic acid (I) was determined in venous blood before the test, during muscular work of 10 or 15 min. (700–900 kgm./min.), and during the rest period of 45 or 50 min. The control series of 37 healthy persons and the experimental series of 30 typical cases of neurocirculatory asthenia (ANC) were each divided into 3 groups according to occupation and degree of training. The resting blood (I) values before the test were normal (3–33 mgm. per cent.) in all the groups. The (I) response showed that the physical fitness of manual workers with (ANC) approximated that of healthy, physically untrained medical students of about the same age. That of chronic cases and the intellectual workers with (ANC) corresponded to that of the healthy, well-trained nurse trainees. The results in the group of control subjects consisting of healthy infantry soldiers show the importance of training in relation to the (I) response. During the rest period the blood (I) values generally underwent a parallel decrease in all the groups. RUTH BERGGREN (Chem. Abstr.).

Influence of the Thyroid on Cerebral Metabolism. Fazekas, Joseph F., et al. Endocrinology, **48**, 169–74 (1951).]

Cerebral cortical (O) consumption was not influenced by hyperthyroidism in young and adult rats nor did hyperthyroidism appear to influence the metabolism of adult rat cortex. An acceleration toward the normal adult metabolic level was observed in hyperthyroid young rats. L. E. GILSON (Chem. Abstr.).

Alcoholism as a Nutritional Problem. Williams, R. J. [*J. Clin. Nutrition*, **1**, 32–6 (1952).]

The conclusion that nutritional deficiency is a basic cause of alcoholism is based on (1) recent findings in the field of biochemical genetics, (2) from direct animal experimentation, and (3) from clinical findings. Experiments on rats showed that their alcoholic consumption increased when fed a marginal diet, low in B vitamins. The alcoholic consumption decreased or vanished completely immediately when the animals were given well-balanced diet. The drinking pattern was maintained as long as the diet furnished all the necessary nutrients. Different strains of animals showed different drinking patterns, some needed substances not supplied by the food, e.g., antibiotics in order to change their drinking pattern.

LILY E. FUCHS (Chem. Abstr.).

Fractions of Brain Substances which Absorb Radiostope Phosphorus^{32}. *Naka, Syuzo, et al.* [*Kyushu Mem. Med. Sci.*, **2**, 63–71 (1951).]

The lecithin and nucleoprotein fraction of brain combined with P^{32} in the form of PO_4 ion at pH 7·6 when incubated at 37° with or without brain homogenate.

J. D. TAYLOR (Chem. Abstr.).

Nerve Stimulation a Resonance Phenomenon? Gäbelein, Klaus. [*Grenzgebiete Med.*, **2**, 521 (1949); *Chem. Zentr.*, **11**, 668 (1950).]

In the theory advanced, the conduction of the nerve impulse is assumed to consist alternately of internodal transport of vitamin B_1 and a transport substance in the transverse nerve membrane. The theory explains such processes as the development of taste, narcosis, and the manner of action of alkaloids and sexual hormones. Taste and the effect of alkaloids are regarded not as chemical processes but rather as physical resonance phenomena. The sensation of taste is determined by the number and location of the π electrons.

M. G. Moore (Chem. Abstr.).

Oxygen Toxicity. Effects in Man of Oxygen Inhalation at 1 *and* 3·5 *Atmospheres upon Blood Gas Transport, Cerebral Circulation and Cerebral Metabolism. Lambertsen, C. J., et al.* [*J. Appl. Physiol.*, **5**, 471 (1953).]

At 3·5 atm., O inhalation by normal men produced a 55 per cent. increase in cerebral vascular resistance which resulted in a 25 per cent. reduction in the blood-flow rate through the brain. These changes were approximately twice as great as those associated with O inhalation 1 atm., but the differences were not statistically significant in the experiment. The amount of O physically dissolved in arterial blood at 3·5 atm. averaged 6·5 volume per cent. However, more O was given up to brain tissue than was present in physical solution in the arterial blood because of the slower rate of cerebral circulation and as a result the average internal jugular hemoglobin saturation at 3·5 atm. was 89 per cent. The removal of most of the physically dissolved O produced pO_2 fall of about 2,000 mm. Hg as blood passed through the brain. Partial interference with the normal reduction of oxyhemoglobin rendered the transport of CO_2 by the blood less efficient. This, with the diminished cerebral blood flow, accounted for an 8 mm. increase in the arteriovenous pCO_2 difference across the brain at 3·5 atm. The elevation of internal jugular pCO_2 was limited to 3 mm. by a 5 mm. fall in arterial pCO_2. This is not compatible with the concept of a marked increase in brain tissue pCO_2 as a contributing cause of O toxicity. No alteration in the O-consumption rate or respiratory quotient of the brain occurred at 1 or 3·5 atm. It is proposed that central accumulation CO_2 on O breathing at increased ambient pressure does not contribute to the toxicity of O, but indirectly reduces the exposure of brain tissue to toxic O-tension levels by producing hyperventilation and cerebral vasconstriction.

Theresa McKee (Chem. Abstr.).

Mobilization of Brain Cholesterol. Laszlo, J., et al. [*Acta Morphol. Acad. Sci. Hung.*, **3**, 33 (1953).]

In degenerative diseases of the brain, cholesterol passes from the brain into the general circulation in four ways: through the lipide granules of cells in the brain capillaries and in the sinuses of the dura, chylomicrons, lipides in endothelial cells of capillaries and corpuscula amylacea. The blood cholesterol is thereby increased.

Erich Heftmann (Chem. Abstr.).

17-*Ketosteroids in Some Mental Diseases. Benvenuti, M., and Parigi, S.* [*Folia Endocrinol.*, **6**, 129 (1953).]

In 46 patients with depression, mania or schizophrenia a normal 17-ketosteroid excretion was observed, with some lower values in the two first diseases.

C. Scandura (Chem. Abstr.).

Amine Oxidase, Pressor Amines and Cholinesterase in Brain Tumors. Bülbring, E., et al. [*Lancet*, **264**, 865 (1953).]

Glia tumors comprised predominantly of glia cells contained as much enzyme activity as normal brain tissue. Amine oxidase activity was about the same order as that in normal brain areas. Cholinesterase activity in 6 of 8 gliomas was greater than that in normal cerebrum due principally to pseudocholinesterase. One glioma (from a 3-year-old child) contained 7·5 γ noradrenaline/gm. (This amount is more than has been found in any area of the normal central nervous system.)

Barbara R. Murray (Chem. Abstr.).

Increased Copper in the Serum of Schizophrenics. Bischoff, A. [*Monatsschr. Psychiat. Neurol.*, **124**, 211 (1952).]

In 90 per cent. of 88 schizophrenics the Cu concentration of the serum was above normal.

Warren M. Sperry (Chem. Abstr.).

Relation of Cortical pH to Hyperoxic Convulsions. Perot, P. L., jun., et al. [*Am. J. Physiol.*, **173**, 158 (1953).]

Cats curarized with dihydro-β-erythroidine-HBr were subjected to high partial pressures of O_2 up to 6 atm. (75 lb. per sq. in. gage). Beginning 2–3·5 minutes after a pressure of 15 lb./sq. in. gage was reached, changes in H concentration of the brain were noted as a change in cortical pH. This increase in acidity continued until a gage pressure of 75 lb./sq. in. was attained when the pH change was 0·25–0·53 units. Shifts in pH toward the acid always occurred prior to the onset of seizures. Only minor changes in pH were noted after pressure was stabilized at 6 atm. unless the pressure was maintained at this level for an extended period of time.

E. D. WALTER (Chem. Abstr.).

Oxygen Tension of the Brain During Hyperoxic Convulsions. Sonnenschein, R. R., et al. [*Am. J. Physiol*, **173**, 161 (1953).]

O tension of the cerebral cortex of cats was determined by the Pt-cathode polarographic method. During a simultaneous increase in both the ambient pressure and the pressure of inspired O from 1 atm. to 6 atm., a rapid rise of 10–50-fold occurred in O tension. After the peak value was reached, a gradual decrease occurred until pO_2 was close to the initial level. Seizures occurred only after the onset of the rapid rise in O tension. E. D. WALTER (Chem. Abstr.).

Effect of the Functional State of the Central Nervous System on the Activity of Proteolytic Enzymes of the Gastrointestinal Canal and Liver in Rats under Conditions of Dietary Deficiency of Protein. Balba, T. Ya. [*Voprosy Pitaniya*, **12**. No. 1, 23 (1953).]

The activity of all enzymes of the digestive tract is unchanged by peroral administration of small doses of caffeine, except for the action of pepsin which declines. Subcutaneous injection of larger doses of caffeine leads to a small decline of erepsin activity. Administration of chloral hydrate causes an increase of trypsin activity, and a decline of liver cathepsin. The experiments were performed with rats on a protein-deficient diet. G. M. KOSOLAPOFF (Chem. Abstr.).

Anaerobic Glycolysis in situ *in Rabbit Brain at Different Temperatures. Thorn, Werner, and Raczkowskil, H. A.* [*Biochem. Z.*, **323**, 21 (1952).]

The anaerobic glycolysis in rabbit brain was followed at 26, 30, and 38° body temperature by determining the lactic acid (I) of the brain after measured periods of glycolysis. (I) accumulates following an induction period of 4–5 seconds at 38°, 15 seconds at 30°, and 35 seconds at 26°. The curve of (I) formation shows 2 bends, at about 40 mgm. per cent. and, again, at 80–90 mgm. per cent. Between these 2 bends the (I) production follows a linear course like a reaction of the first order, with consistences in the ratio of 2·5–3·0 : 1·35 : 1·0 at the different temperatures. After the second inflection the curve is still linear, but the rate is reduced to about $\frac{1}{8}$ of the previous rate. The Q_{10} of the velocity consistences under the three temperatures is 2·5. S. MORGULIS (Chem. Abstr.).

Metabolism and the Central Nervous System. Berenshtein, F. Ya. [*Uspekhi Sovremennoĭ Biol.*, **34**, 367 (1952).]

A review with 103 references. JULIAN F. SMITH (Chem. Abstr.).

Histochemical Studies of the Brain. Shiko, Takeya. [*Acta Pathol. Japonica*, **1**, 30 (1951).]

In sections of brain, chiefly pallidum, a compound pseudolime, a conglomerate easily stained with hematoxylin, was found to be different from other tissues by the use of various reactions. By taking advantage of different dissolving abilities of various organic solvents, the medullary sheaths of the brain were found to consist of one substance stained by Sudan (III) and a fatty envelope characterized by positive Sugamo staining. Another substance, brain lipofuscin, was also studied.

J. D. TAYLOR (Chem. Abstr.).

Pyruvate Oxidase System in Brain Tissue. Peter, R. A., and Wakelin, R. W. [*J. Physiol.*, **119**, 421 (1953).]

Pigeon brain homogenates, prepared by the method of Banga *et al.*, showed decreased O_2 uptake in the presence of fluorocitrate (I), the selective inhibitor for aconitase, with simultaneous large accumulations of citrate (II). Brei preparations showed only a small accumulation of (II) induced by (I), with no measurable O_2 uptake. *In vivo* injections in doses as small as 20γ, but usually 150–200γ, into the subarachnoid space of the right cerebral hemisphere in pigeons of about 300–350 gm. body weight, resulted in death following opisthotonus and convulsions, accompanied by a large accumulation of (II). Larger doses of fluoroacetate (III) or injections of similar doses of (II) produced neither convulsion nor (II) accumulation. This emphasized the significance of (I) in (III) poisoning. All data presented indicate (1) the lethal nature of enzymic synthesis in (III) poisoning; (2) that citric acid is on the direct path of pyruvate oxidation in the brain, *in vivo*; and (3) that the brain pyruvate oxidase system studied comprises the pyruvate dehydrogenase plus the enzymes of the tricarboxylic acid cycle.

Morris Rockstein (Chem. Abstr.).

The Cathepsic Activity of the Central Nervous System. Calabi, V. [*Riv. patol. nervosa e mentale*, **69**, 104 (1948); *Excerpta Med.*, Sect. VIII, **2**, 803 (1949).]

Cathepsin-like proteolytic enzymes in the central nervous system were studied by determining the autoproteolytic activity of brain tissue from various animals by calculating the N content of the trichloroacetic acid ppt. from the glycerin extract before and after incubation at pH 4·2 at 37°. The N decreased about 25 per cent., indicating active proteolysis similar to that observed in liver tissue. The enzyme action was not activated by ascorbic acid or cysteine.

W. C. Tobie (Chem. Abstr.).

The Penetration of Phosphorus^{32} *into the Nervous Tissues of the Rabbit. Brierley, J. B.* [*J. Physiol.*, **116**, 24P (1952).]

Injection of histamine resulted in increased penetration of $P^{32}O_4^{-3}$ into the extracellular fluid of the spinal ganglia, sciatic nerve, spinal cord, medulla, hypothalamus, hippocampus and cortex, probably by increasing the capillary permeability to PO_4^{-3} ions.

Morris Rockstein (Chem. Abstr.).

The Role of Urea in Brain Swelling. Ambo, Hisashi. [*Acta Pathol. Japonica*, **1**, 205 (1951).]

Urea, demonstrated by the xanthydrol method, was present in the brains of patients with signs of brain pressure, but not in brains of normal patients. In rabbits with brain swelling produced by chronic administration of hepatoxic agents in small doses urea was also present.

J. D. Taylor (Chem. Abstr.).

Further Studies on the Neurolytic Properties of the Spinal Fluid in Health and Disease. Kovacs, Ernest. [*Can. J. Med. Sci.*, **31**, 109 (1953).]

With bovine brain-cord pulp as substrate buffered at pH 8·5 or pH 5·5 and incubated at 37° for 24 hours, neurolytic enzymes in cerebrospinal fluid (I) were shown to split the substrate to form acid-solution phosphate and reducing substances. Three main groups of cases were distinguished: normal patients with negative laboratory findings in (I)—no neurolytic activity; patients with inflammatory processes in the central nervous system with pathological changes in (I)—highly neurolytic activity; patients with generative and proliferative processes, moderate changes in (I)—high neurolytic activity.

J. D. Taylor (Chem. Abstr.).

Nature of Specific Sensitivity to Oxygen Deficiency in the Brain. Shapot, V. S. [*Uspekhi Sovremenoĭ Biol.*, **34**, 244 (1952).]

Effects of hypoxia and anoxia in brain tissue are reviewed with respect to reactions of amino N, phosphate P, adenosine phosphates, and lactic acid.

Julian F. Smith (Chem. Abstr.).

Cerebral Hemodynamics in Cerebral Arteriosclerosis. *Fazekas, Joseph F., et al.* [*J. Gerontol.*, **8**, 137 (1953).]

Cerebral hemodynamics and O consumption of persons 50 years or older having cerebral arteriosclerosis with or without hypertension were studied before and during inhalation of 5 per cent. CO_2 or intravenous administration of aminophylline during hyperventilation. The changes in cerebral blood flow, O delivery, and cerebral vascular resistance were similar, but less marked than those in younger subjects, and the response was the same in both normotensive and hypertensive subjects. THERESA MCKEE (Chem. Abstr.).

Anatomical Changes in the Brain in Schizophrenia. *Vogt, C., and Vogt, O.* [*Artzl. Forsch.*, **3**, 121 (1949); *Excerpta Med.*, Sect. VIII, **2**, 806 (1949).]

Mainly pathological and histological. There may be an increase in Feulgen-negative nucleoproteins provoked by a decrease of Nissl substance in the nerve cells, accompanied by an enlargement of the nucleolus which is composed of the same nucleoproteins. This is a sign of repair of pathological conditions.

W. C. TOBIE (Chem. Abstr.).

Experimental Swelling of the Brain and its Bound Water Content. *Ambo, Hisashi.* [*Acta Pathol. Japonica*, **1**, 63 (1951).]

Typical cerebral swelling as well as cerebral edema was produced in rabbits with time by ligation of the jugular vein, vena cava inferior and ureters, and by poisoning with $HgCl_2$, $K_2Cr_2O_7$ $CHCl_3$ $CHCl_4$, and yellow P. The bound and free H_2O (I) were determined by the $CoCl_2$ method of Hatschek (*C. A.*, **30**, 5096^6). Normal rabbit brain contained 7·0–7·5 per cent bound and 68–69 per cent. free (I). In cases of cerebral swelling the bound (I) increased to 8·2–9·6 per cent. with a lessening of free and total (I). In cerebral edema bound (I) did not increase, but free (I) increased to 70–72 per cent.

J. D. TAYLOR (Chem. Abstr.).

Effects of d-Amphetamine on the Electroencephalogram of the Dog. *Schallek, Wm., and Walz, Donald.* [*Proc. Soc. Exptl. Biol. Med.*, **82**, 715 (1953).]

Tracings and discussion. L. E. GILSON (Chem. Abstr.).

Effect of Antihistamine Substances on Brain Respiration. *Domonkos, J., and Huszak, I.* [*Acta Physiol. Acad. Sci. Hung.*, **4**, 25 (1953).]

Antihistamines (pyribenzamine, neoantergan, or antistine) inhibit the reduction of cytochromes. W. H. FISHMAN (Chem. Abstr.).

Anaerobic Reactions of Phospholipins in Brain Suspensions. *Sloane-Stanley, G. H.* [*Biochem. J.*, **53**, 613 (1953).]

Suspensions of guinea-pig brain were incubated under N_2 with lipide rich in phosphatidylserine at pH 5–9. The evidence for decarboxylation of the phosphatidylserine to phosphatidylethanolamine is not conclusive, and this reaction could not occur at a greater rate than 2·4 micromoles per gm. wet wt. per hour. None of the nitrogenous lipides was rapidly hydrolyzed, but there was evidence for the existence of an active enzyme system in brain capable of hydrolyzing the diphosphoinositide fraction of the brain cephalins, and that the system involves at least 2 enzymes. Brain lipide samples were incubated under a mixture of 95 per cent. N_2, 5 per cent. CO_2 (vol./vol.) with suspensions ot guinea-pig brain in a $NaHCO_3$ solution of about pH 7·4. The evolution of CO_2, in excess ot that from brain homogenates alone, suggests that free acid was formed from the hydrolyzed lipides. It was found that the "inositol phosphatide" fraction, containing about 40 per cent. of the diphosphoinositide, reacted nearly 10 times as rapidly as any other lipide fraction (66 micromoles per gm. wet wt. per hour). The main reaction seems to have been a partial hydrolysis of diphosphoinositide.

S. MORGULIS (Chem. Abstr.).

Hypothalamic Involvement in the Pituitary-adrenocortical Response to Stress Stimuli. Porter, R. W. [*Am. J. Physiol.*, **172**, 515 (1953).]

Eosinopenic response to adrenaline, formalin and histamine was measured before and after making hypothalamic lesions in cats. Anterior lesions were without effect; posterior lesions prevented the eosinopenic response. In other experiments, exploration stimulation of the hypothalamus was undertaken and the level of circulating eosinophils determined. Eosinopenia resulted from excitation of tuberal and mammillary areas; surrounding regions did not induce this response. Results support participation of the central nervous system in the pituitary-adrenal response. E. D. WALTER (Chem. Abstr.).

Effect of the Higher Nervous Activity on Development of Experiment Tumors. Kozhevnikova, E. P. [*Arkh. Patol.*, **15**, No. 1, 22 (1953).]

Mice under conditions of nervous strain (noise stimuli) treated cutaneously with methylcholanthrene show some 3-fold increase in the incidence of tumors over the control animals. Hence hypertension of the higher nervous system is conducive to development of malignant growths. G. M. KOSOLAPOFF (Chem. Abstr.).

Degenerative Changes in the Central Nervous Fibers in the Production of Hypercholesterolemia. Shumova, N. T. [*Arkh. Patol.*, **10**, No. 6, 28 (1948); *Abstracts World Med.*, **6**, 229 (1949).]

Hypercholesterolemia (I) can be produced in dogs by injury to the central nervous system. Degeneration in myelinated nerve fibers containing cholesterol (II) is associated with increased (II) in the circulation. Similar changes occur in humans with lipide-storage diseases, neurosyphilis and lipide nephrosis. In decerebrate dogs, after removal of both cerebral hemispheres, no (I) can be produced, but blood (II) can be made to rise steeply if one hemisphere is intact. After partial cortical extirpation, (I) occurred in 5 of 6 dogs. The rise in (II) was greatest in blood from veins draining the brain and was proportional to the amount of demyelination. Regeneration of nerve fibers often proceeds at the same as degeneration and may account for the increased (II) in the brain found by some workers.
W. C. TOBIE (Chem. Abstr.).

Electrophoretic and Chemical Serum-protein Fractions in Multiple Sclerosis. Saifer, A., et al. [*Am. J. Med. Sci.*, **225**, 287 (1953).]

About 90 per cent. of 23 patients with multiple sclerosis showed the following typical electrophoretic serum-protein pattern: significantly decreased albumin and albumin/globulin ratio, increased α_2- and β-globulin fractions, slightly elevated or normal γ-globulin, and normal α_1-globulin. In the remaining 10 per cent. of patients, most but not all of these characteristics were present. Various tests for serum-protein fractions that may have value in diagnosis of multiple sclerosis are discussed.
MARION HORN PESKIN (Chem. Abstr.).

The Pathology of Disseminated Sclerosis. Huszàk, I., and Szák, J. [*Orvosi Hetilap*, **90**, 201 (1949); *Excerpta Med.*, Sect. VIII, **2**, 805 (1949).]

Previous work by H. is reviewed. Cytochrome oxidase is the O-activator of the grey matter; cuproprotein has the same function in the white matter of the central nervous system. Human and horse brains contain a dialyzable substance which increases the coagulation time of plasma; more is found in the grey than in the white substance. Differences in coagulation time probably result from differences in the amount of heparin, not kinase. The frequency of thromboses in the white matter is attributed to greater amounts of heparin.
W. C. TOBIE (Chem. Abstr.).

New Researches on Multiple Sclerosis. Gokay, F. K. [*Bull. fac. med. Istanbul*, **11**, 109 (1948); *Excerpta Med., Sect.* VIII, **2**, 753 (1949).]

Based upon the theory that multiple sclerosis is caused by a neurotropic virus, the main pharmacological agents used in treatment are Na salicylate and $Hg(CN)_2$. Good results are claimed. W. C. TOBIE (Chem. Abstr.).

Dihydroergotamine (*D.H.E.* 45) *in Ophthalmic Migraine and Glaucoma. Persichetti, C.* [*Boll. oculist.*, **29**, 234 (1950) ; *Am. J. Ophthalmol.*, **34**, 132 (1951).]

Intramuscular injections of dihydroergotamine (I) in 7 normal controls caused no changes in retinal arterial or intraocular pressure, but in 5 cases there was a slight drop in the brachial arterial pressure. Taken orally 3 times a day for 4–5 days, (I) had little effect on arterial pressures. Results (which are described) in ophthalmic migraine and glaucoma varied widely. There was no correlation between arterial pressures and good therapeutic results.

W. C. Tobie (Chem. Abstr.).

The Effect of " Agene-induced " Convulsions on Adrenal Steroid Excretion in Normal and Castrate Dogs. Costa, P. J., and Bonnycastle, D. D. [*J. Endocrinol.*, **9**, 76 (1953).]

Daily oral feeding of 0·6 gm. of agenized zein (40 gm. NCl_3/50 kgm. zein.) per kgm. body weight to 18 male dogs for 2 days caused convulsions in all within 48 hours (the pre-fit period). About half of the dogs died. During the normal, pre-fit, and fit periods, respectively, average urinary 17-ketosteroid excretions per 24 hours were 1·91, 1·44, and 0·91 mgm. During the normal period, first and second pre-fit days, and the fit period, reducing corticoids averaged 0·89, 1·19, 0·37, and 0·28 mgm./day, respectively. Castrate dogs showed similar reaction patterns. The expected increase in steroid excretion following stress was not seen in these studies. Convulsions following metrazole or insulin administration did, however, produce significant increases in steroid excretion.

Kathryn Knowlton (Chem. Abstr.).

2. Pharmacology and Treatment.

Curare and Shock. Imperati, L., et al. [*J. Intern. Coll. Surgeons*, **13**, 54 (1950) (*in English*).]

Previous work is reviewed. Experiments on animals are outlined. Moderate repeated doses of curare prevent shock, probably by altering the acetylcholinesterase system. Curare raises the blood pressure in animals in serious shock.

W. C. Tobie (Chem. Abstr.).

Effect of Depressants on the Metabolism of Stimulated Cerebral Tissues. McIlwain, H. [*Biochem. J.*, **53**, 403, (1953).]

Depression of activity of the central nervous system by barbiturates involves a fall in respiration, lactic acid, and inorganic phosphate and a rise in phosphocreatine. Phenobarbital, butethal, allobarbital, and chloral have practically no effect on the respiration of sections of rat or guinea-pig cerebral tissue in concentrations less than 10^{-3} M but do so when the tissue is electrically stimulated, and the inhibition is reversed when the drug is removed. Likewise, stimulation by K salts or 2,4-dinitrophenol increases the sensitivity of respiration of the cerebral cortex to depressants. Atropine affects selectively electrically stimulated tissues. Depressants also decrease the lactic acid formed from glucose by electrically stimulated cerebral tissues.

S. Morgulis (Chem. Abstr.).

Comparative Action of E.C.T. (*Electric Convulsion Therapy*) *and Pituitary Anterior Lobe Hormones on Thyroid Function. Reiss, M., et al.* [*Brit. Med. J.*, ii, 634, (1951.]

Thyroid activity was studied with I^{131}. E.C.T. increased the activity of hypoactive thyroids, reduced the activity of hyperactive thyroids, and usually lowered the activity of normal thyroids. Treatment with thyrotropic hormone brought subnormally active thyroids within the normal range. Thyroid activity was reduced by treatment with adrenocorticotropic hormone or with testosterone, estrone, or both.

Marshall E. Deutsch (Chem. Abstr.).

Relaxant of Very Brief Action. Scurr, C. F. [*Brit. Med. J.*, **11**, 831 (1951).]

After rapid injection of 50–75 mgm. di-(β-ethyldimethylammoniummethyl) succinate diiodide into an adult, paralysis ensues for not more than 2½ minutes.

Marshall E. Deutsch (Chem. Abstr.).

Standardization of Potency and Toxicity of Anticonvulsants. III. Frommel, Ed., et al. [*Arch. intern. pharmacodynamie*, **92**, 44 (1952).]

A comparison of the effectiveness of drugs against coramine, strychnine or metrazole convulsions in several species of animal, as judged by their therapeutic index (amount causing 5 per cent. deaths/amount giving 95 per cent. protection) showed that a mixture (M 551) of 5 parts (ethylphenylacetyl) urea (S 46) with 1 part of phenylacetylurea, and S 46 are much better than phenobarbital or the hydantoins, but the action of phenobarbital is longer. In the mouse after strychnine the index was M 551, 16·7; S 46, 10·3; dimethyldithohydantoin 7·9; phenobarbital 6·3; methylethylphenylhydantoin 4·7; trimethyloxazolidinedione 4·6; and phenylacetylurea 4·5. S 46 in the rabbit does not counteract the hyperglycemia of metrazole shock, but phenobarbital does; the latter, and M-551, prevent the rise of blood Ca or inorganic P, and the fall in the alkali reserve of the blood. The formed elements are not much affected. M. L. C. Bernheim (Chem. Abstr.).

Pentamethylenetetrazole (Metrazole). Radouco, C., et al. [*Arch. intern. pharmacodynamie*, **92**, 13–38 (1952).]

In the rabbit, metrazole shock increases the blood levels of sugar, Ca, and inorganic P, and decreases the alkali reserve. It causes changes in the hematocrit and the formed elements. There are neurovegetative changes as well as pyramidal and extrapyramidal excitation. The nerve changes are of much shorter duration than the metabolic effects. M. L. C. Bernheim (Chem. Abstr.).

Action of Synthetic Curare-like Substances on Convulsions Produced by Cardiazole. Verga, G. [*Boll. soc. ital. biol. sper.*, **24**, 197 (1948).]

The 2 synthetic curare-like substances studied were 1,2-dihydroxy-3-o-tolyloxypropane and 1,2-dihydroxy-3-o-anisyloxypropane; both exert a protective action against convulsions induced in rabbits by cardiazole. B. A. (Chem. Abstr.).

The Effects of High Oxygen Atmospheres on Drug-induced Convulsions. Cotten, M. de V., and Walton, R. P. [*Anesthesiology*, **12**, 491 (1951).]

In each experiment 10 animals which received injections of drugs were observed in a high O atmosphere, and 10 animals similarly injected were studied simultaneously in ordinary room air; 36 such experiments were conducted with rats and mice. Metrazole was used in 15 experiments, strychnine sulfate in 12, and NaCN in 12. In addition two similar experiments with metrazole and two with strychnine were conducted in which the effects of 15 per cent. O atmosphere were contrasted with those of ordinary air. High O atmospheres, as compared with ordinary room air, prolonged the survival time but with continuance of convulsions. These time periods were somewhat more than doubled as calculated from an over-all average with the three drugs. Survival rates were not considered statistically different in the two types of atmospheres. Pulmonary hemorrhage was consistently observed and was more prominent in those animals maintained in high O atmospheres with corresponding longer intervals of convulsions. Results in 15 per cent. O atmospheres did not differ significantly from those in ordinary air, except possibly for a shorter survival interval in the 15 per cent. O atmosphere. Experiments with dogs receiving large intravenous doses of strychnine failed to show that antifibrillatory drugs have any particular indication in these conditions. These experiments, insofar as their implications can be transferred to clinical conditions, indicate a definite but limited advantage in the administration of O by mask during intervals between critical recurrent convulsions.

Ruth Berggren (Chem. Abstr.).

Blood Flow and Oxygen Consumption of the Human Brain During Anesthesia Produced by Thiopental. Wechsler, R. L., et al. [*Anesthesiology*, **12**, 308 (1951).]

The effects of the intravenous administration of Na thiopental (I) in anesthetic doses were studied on blood gases, blood pH, cerebral blood flow, cerebral O_2 consumption, and cerebrovascular resistance. (I) significantly depressed cerebral utilization of O_2 in spite of the maintenance of an adequate blood flow. No statistically significant difference was noted in the values obtained from the right or left internal jugular veins under anesthesia. Thus, there is adequate mixing of cerebral venous blood from cortical and subcortical areas before it enters the jugular veins. RUTH BERGGREN (Chem. Abstr.).

Cholinesterase of Blood and of the Nervous Tissue after Shock Treatments, in Humans and Animals. De Caro, Diego. [Riv. neurol., **20**, 23 (1950).]

In 53 patients (blood) and in 34 rabbits (blood and cerebral tissue) no significant changes of the cholinesterase activity were observed after shock treatments. C. SCANDURA (Chem. Abstr.).

Experimental Convulsions and Antiepileptic Drugs. Cheymol. J. [Actualitiés pharmacol., **2**, 1–55 (1950).]

The pathological and physiological aspects of experimental and other convulsions in man and animals are discussed. The pharmacology of antiepileptic and anticonvulsive drugs is reviewed with respect to chemical composition and mode of action. W. C. TOBIE (Chem. Abstr.).

Synergic Effect on the Respiratory Function and Antagonistic Effect on the Central Nervous System of Caffeine associated with Barbiturates. Tiffeneau, Robert. [Thérapie, **4**, 141–5 (1949).]

The intensity of acetylcholine induced bronchospasms of guinea pigs was decreased more by the simultaneous injection of 20 mgm./kgm. of butylethylmalonylurea and 80 mgm./kgm. of caffeine than by the injection of either alone. G. SAG (Chem. Abstr.).

Effects of Frontal Leucotomy on the Anorexia Produced by Benzedrine. Di Ferrante, N., and Longo, V. G. [Farmaco, Ed. sci. (Pavia), **8**, 16 (1953).]

The anorexic action of benzedrine (I) is pronounced in the dog, less so in the rat, and insignificant in the chick, which shows that the development of the forebrain is a deciding factor in this response. Morphine, strychnine, atropine, phenergan, and hydergin did not modify the effect of (I). In dogs subjected to frontal leucotomy benzedrine, given at ordinary doses, did not interfere with the appetite, but higher doses were still effective. A. E. MEYER (Chem. Abstr.).

The Effects of Priscoline on Cerebral Circulation and Metabolism. Scheinberg, P., et al. [J. Clin. Invest., **32**, 125 (1953).]

Intravenous priscoline, in doses of 50–100 mgm., administered in 15 to 20 minutes, results in an apparent though not statistically significant decrease in cerebral blood flow, an increase in cerebral venous O difference and venous glucose difference, a slight difference in mean arterial pressure, a decrease in arterial CO_2 content and arterial pCO_2, a rise in arterial pH, with no alteration in cerebral O consumption, cerebral glucose consumption, cerebral vascular resistance, arterial O saturation, arterial pO_2, and cerebral venous pO_2. It is postulated that priscoline produces mild cerebral vasoconstriction and slight hypoxia of brain tissue, though its effects are variable. This study does not explain the reported beneficial clinical effects of priscoline in cerebral vascular disease.

JOHN T. MYERS (Chem. Abstr.).

Poisoning by Methylparafynol (Dormison). Fatal Suicidal Overdose of 3 *methyl* 1-*pentyn*-3-*ol, a New Hypnotic. Cares, Rueben M., et al. [Am. J. Clin. Pathol.,* **23**, 129 (1953).]

JOHN T. MYERS (Chem. Abstr.).

The Mechanism of the Effect of Apomorphine and of Nicotinamide-adenine in the Treatment of Chronic Alcoholics. Lecoq, Raoul. [Thérapie, **7**, 327–36 (1952).]

Na pyruvate (I) was prepared (Howard and Fraser, *C. A.*, **20**, 45) but insufficiently washed with EtOH. Rabbits weighing 1·8–2·0 kgm. were intoxicated by ingestion of 0·5 gm. of tetraethylthiuram disulfide (II) followed in one hour by an intravenous injection of 20 ml. of isotonic glucose solution containing 25 per cent. EtOH or 0·25 gm. of (I). Death followed in both cases in 2–3 minutes. Apomorphine-HCl (III), 0·1 gm., protected the rabbits against EtOH but was ineffective against (I). In the same conditions, injection of nicotinamide, 15 mgm., and of adenine, 25 mgm., prevented any fatal poisonings, probably by favoring biosynthesis of coenzymes (I) and (II). AcH and pyruvic acid were determined in rabbits by the Stotz (*C. A.*, **37**, 5751^{8}) and by the Friedmann-Haugen (*C. A.*, **37**, 2401^{4}) methods, respectively. The blood of control animals contained 1–2 mg./l. of AcH and 5–10 mgm./l. of pyruvic acid. Corresponding values, 15 minutes after application of (II) and EtOH were 3·5 and 15·4; 45 minutes later 3·7 and 21·1 mgm./l. In animals protected with (III) 15 mintues after EtOH injection the blood contained AcH 3·6 and pyruvic acid 4·2 mgm./l.; after 1 hour these values were 4·1 and 7·7 mgm./l. When the prevention was performed with adenine, the 15-minutes AcH and pyruvic acid levels were 6·5 and 8·4 mgm./l., and the 1 hour levels 7·3 and 14·3 mgm./l. The impure (I), 0·2 mgm., had a lethal effect on rabbits in 5–20 minutes, while compound pyruvic acid was inoffensive even in doses of 0·6 gm., given either alone or after (II) and EtOH. If the EtOH used for washing (I) was evaporated and the residue (in a physiological solution), was injected into a rabbit, a temporary epileptiform crisis resulted in 2–3 minutes. If the animal received after this treatment 0·25 gm. of pure (I), death followed in a few minutes. The formation of an unknown "complementary pyruvic factor" is admitted during oxidation of tartaric acid. Malonic acid had a similar potentiating effect on pyruvic acid, but to a lesser degree. G. Sag (Chem. Abstr.).

Antiepileptic Drugs. I. Kaufman, Charles, and Isenberg, Sydney. [*Med. Clinics N. Am.*, **36**, 1381–92 (1952).]

Hydantoins, oxazolidine-2,4-diones, barbiturates, and acetylureas are discussed with reference to pharmacological action, therapeutic indication and mode of application. Erich Heftmann (Chem. Abstr.).

The Hypnotic Action of Antihistaminics. Tanake, Kiyoshi. [*Folia Pharmacol. Japon.*, **47**, No. 2, 30–2 (1951).]

Benadryl hardly shows hypnotic action in rabbits, mice and children; this suggests a close relation with brain development. In rabbits a hypnotic action appears when applied directly to the sleeping centre or its vicinity in the brain. By ordinary injections the other parts of the brain appear to be excited simultaneously so that other excitations suppress that of the sleeping center. Injections after administration of urethan produce further hypnosis in rabbits.

S. Kitoaka (Chem. Abstr.).

Secondary Circulatory Shock in Rats with Severe Barbituric Acid poisoning. Kirkegaard, Aage. [*Acta Pharmacol. Toxicol.*, **8**, 315–28 (1952).]

If rats given 6–7 times the lethal dose of allylisopropylbarbituric acid were subjected to artificial respiration their survival time was lengthened by about three hours and the rats gradually developed a secondary circulatory shock with hemoconcentration. Injection of rat blood or serum prolonged their survival still more.

L. E. Gilson (Chem. Abstr.).

The Antabuse Effect of Some Compounds Related to Antabuse and Cyanamide. Hald, Jens, et al. [*Acta Pharmacol. Toxicol.*, **8**, 329–37 (1952).],

The compounds (given orally) were tested for ability to induce accumulation of MeCHO in rabbits after intake of EtOH. A marked and prolonged effect was found after tetramethyl- and tetraethylthiuram disulfide and tetramethyl- and tetraethylthiuram monosulfide. Some effect was seen after cyanamide. Thiuram disulfide and tetrapropyl- and tetrabutylthiuram disulfide showed only a slight effect or none. No effect was seen with dicyanodiamide and dixanthogen. Diethylcyanamide was too toxic to be tested satisfactorily.

L. E. Gilson (Chem. Abstr.).

Antabuse Treatment and Ether Anesthesia. Hald, Jens, and Larsen, Valdemar. [*Acta Pharmacol. Toxicol.*, **8**, 338–42 (1952).]

Rabbits were pretreated with antabuse and made to breathe air containing 6 per cent. by volume of Et_2O vapor. There was no significant rise in the blood MeCHO level and no MeCHO in the expired air.

L. E. Gilson (Chem. Abstr.).

Depressant Action of Inert Gases on the Central Nervous System in Mice. Carpenter, Frank G. [*Am. J. Physiol.*, **172**, 471–4 (1953).]

The depressant actions of N, A, SF_6 and N_2O were measured by the partial pressures of the gases which abolished the response following supramaximal electroshock in mice. The partial pressures that protected 50 per cent. of the mice studied were 265 lb./sq. in. of N, 185 lb./sq. in. of A, 27·5 lb./sq. in of SF_6, and 8·6 lb./sq. in. of N_2O. E. D. Walter (Chem. Abstr.).

Anticurare Action of 3-hydroxyphenyldimethylethylamonium Bromide. Garcia-Valdescasas, F., et al. [*Arch. inst. farmacol. exptl.* (*Madrid*), **4**, 67–80 (1952).]

The potentiating action of the compound (I) towards acetylcholine parallels its anticurare action toward tubocurarine (II) when tested on the rectus muscle of the frog. The anticholinesterase action of (I) is considerably inferior to that of neostigmine but their antagonism to (II) is equal. The effect cannot be explained by an antiesterase action. It is efficacious to counteract the effects of (II) decamethonium and flaxedil, has no muscarine-like action, is of quick action, low toxicity and rapid excretion. A. E. Meyer (Chem. Abstr.).

A New Hypnotic : Dormison. Gialdroni, G., and Crassi, C. [*Atti soc. lombarda sci. med. e biol.*, **7**, 90–7 (1952).]

The therapeutic coefficiency of this drug is favorable. It does not modify the respiration nor influence the cardiovascular system. It effect is counteracted by caffeine and benzedrine but not by strychnine or cardiazole. Experiments *in vitro* show a muscle-relaxing effect. A. E. Meyer (Chem. Abstr.).

Mechanism of the Prevention of Nicotine Convulsions by Hexamethonium and by Adrenaline-blocking Agents. Laurence, D. R., and Stacey, R. S. [*Brit. J. Pharmacol.*, **8**, 62–5 (1953) ; *cf. C. A.*, **46**, 6271*f*.]

Hexamethonium, dibenamine, SKF 688 A, yohimbine, ergotamine, and dihydroergotamine protected mice and rats against nicotine (I) convulsions. Tolazoline, diparcol and artane had a similar weaker action. These substances did not prevent leptazol convulsions. Adrenalectomized rats were protected less effectively than were normals. The simultaneous administration of adrenaline or noradrenaline increased the convulsant action of (I) and leptazol ; pitressin increased the action of leptazol ; it increased that of (I) preceded by hexamethonium. Conclusion : The action of (I) on the brain is intensified by the sympathetic discharge it causes. Sympathetic blockade reduces its convulsant action. The central mechanism is discussed and it is concluded that the vascular changes produced are of major importance. In comparing the potency of drugs action on the central nervous system, the condition of the cerebral circulation should be comparable.

Richard F. Riley (Chem. Abstr.).

Pharmacology of Succinylcholine. Somers, G. F. ' [*Brit. J. Pharmacol.*, **8**, 19–21 (1953).]

In the cat, succinylcholine (I) like decamethonium first increased then briefly paralyzed the indirectly excited maximal twitch response of the anterior soleus and tibialis muscles. Neostigmine increased and prolonged the paralyzing action of (I). (I) showed only the nicotinic actions and not the muscarinic actions of acetylcholine. Richard F. Riley (Chem. Abstr.)

Effects of Adrenaline and Noradrenaline on Electrically Induced Seizures. Minz, Bruno, and Domino, E. F. [*J. Pharmacol. Exptl. Therap.*, **107**, 204–18 (1953).]

The effects of adrenaline, noradrenaline, amphetamine, neosynephrine, pitressin, acetylcholine, nicotine, histamine, glucose, adrenocorticotropin and cortisone on electrically induced seizures were investigated in cats by simultaneous recording of the blood pressure and the electronencephalogram. The results are discussed.

L. E. Gilson (Chem. Abstr.).

Analeptics with Antagonistic Effect on Barbituric Acid Derivatives. Kantemir, I. [*Turk Ijien Tecrübi Biol. Dergisi* (*Turk. Bull. Hyg. Exptl. Biol.*), **12**, 56 (1952).]

The literature about the application of analeptics in poisoning with barbituric acid derivatives is reviewed. Metrazole has a rapid but short effect, while coramine shows a slower but lasting action. Combined administration of strychnine and ephedrine can also be useful in intoxications with barbituric acid derivatives.

Z. Stary (Chem. Abstr.).

Antiepileptics. Werner, G. [*Scientia pharm.*, **20**, 156–63 (1952).]

Review with 27 references on the types of epilepsy and the agents used in treating them. John Howe Scott (Chem. Abstr.).

Present State of Research in Migraine and its Chemotherapy. Hinterstoisser, F. [*Osterr. Apoth.-Ztg.*, **6**, 678–82 (1952).]

A review. Edward H. Sheers (Chem. Abstr.).

The Possibilities of Diminishing the Toxicity of Disulfirum (*Tetraethylthiuram Disulfide*). *Lecoq, Raoul.* [*Thérapie*, **7**, No. 1, 17–20 (1952).]

A review with 27 references. G. Sag (Chem. Abstr.).

The Possible Use of Nissl Substance in the Treatment of Schizophrenia and Neuroses (*a Physiocytological Approach*). *Kubanek, Joseph L.* [*Intern. Record of Med.*, **165**, 479–83 (1952).]

Schizophrenic patients are less able to utilize O_2 probably because of the deficient nucleoprotein embodied in the Nissl bodies of the brain and of sympathetic ganglion cells. Treatment with malononitrile enhances O_2 metabolism and favours restoration of nucleoproteins in central nervous system. J. Dufrenoy (Chem. Abstr.).

Action of Electroconvulsive Therapy on Oxidation-reduction Processes. Mule, F. [*Clin. nuova* (*Rome*), **8**, 482–90 (1949) ; *Excerpta Med.*, Sec. VIII, **3**, 8 (1950).]

Comparisons of the mental condition (in 30 cases) with oxidation-reduction potential, and values for oxidized glutathione indicate that low rH corresponds to the comatose postconvulsive state. W. C. Tobie (Chem. Abstr.).

Influence of Barbiturate on the Sympathetic Nervous System. Trethewie, E. R. [*Med. J. Australia*, **1**, 100 (1953).]

Stimulation of the splanchnic nerve of adrenalectomized cats under chloralose anesthesia caused peripheral vasoconstriction and increased blood pressure. This response was inhibited by Na pentobarbitone (I). Peripheral stimulation of the cut nerve under similar conditions also produced an increase in blood pressure, abolished by (I). If the adrenal glands were removed, the vasopressor response to splanchnic nerve stimulation was greatly impaired by (I). In human subjects the administration of (I) or more particularly of phenobarbital reduced the basal metabolic rate and caused peripheral vascular dilatation.

W. Donald Graham (Chem. Abstr.).

Effects of Coumarin and Benzoxazolones on the Central Nervous System. Mercier, J., et al. [*Ann. pharm. franç.*, **11**, 169 (1953).]

Benzoxazolone and its derivatives have hypnotic, analgesic and hypothermic actions. Oral doses of coumarin (I), 4-methylcoumarin (II), and 7-methylcoumarin

(III) cause in rats in decreasing order elevation of the threshold for electroshock and for metrazole convulsions. In the same order the dose required to produce somnolence, muscular incoordination and paralysis of the hind legs, the doses being 0·05 to 0·5 gm. per kgm., increases. The hypothermic effect also decreases from (I) to (II) to (III). (I) produces in the dog in chloralose anesthesia after oral medication, a progressive fall in blood pressure (0·3 to 0·6 gm. per kgm.), mild bradycardia and considerable respiratory depression. (I) exerts on the gastrocnemius muscle of the dog, stimulated by faradic current, a depressant effect similar to that of myanesin. A. E. MEYER (Chem. Abstr.).

Narcotics and Biological Acetylations. Johnson, W. J., and Quastel, J. H. Nature, **171**, 602 (1953).]

It is shown that inhibition of respiration brought about by a narcotic is accompanied by a decreased rate of acetylation, and that the addition of adenosine triphosphate (I) to an aerobic system alleviates the narcotic effect on acetylation. The effect of added (I) indicates that the narcotic inhibition of acetylation is the result of a suppression of the oxidative synthesis of this ester. It is apparent that narcotics at high concentrations affect neither the acetylating enzymes *per se*, nor the pyruvate dismutation system, nor the glycolytic sequence in beef-brain extract. Thus the narcotics do not inhibit the utilization of (I) in these metabolic processes. W. J. PETERSON (Chem. Abstr.).

The Effects of Muscle Relaxants on the Respiratory Center. Frey, R., et al. [*Der Anasthesist,* **1**, 33 (1952).]

The effects of d-tubocurarine, dimethyl-d-tubocurarine, flaxedil, deoxydauricin, decamethonium, succinylcholine and guaiacol glycerol ether on the respiratory center of artificially respirated dogs were studied by observing simultaneously the action potentials of the phrenic nerve, diaphragm and heart and the respiratory pattern. Circulatory status and alveolar CO_2 were held constant. In addition to the peripheral effects the muscle relaxants showed central effects characterized by a very short stimulatory phase followed by central depression, the duration of which varied with the particular drug and became significant only with abnormally high dosage. KARL F. URBACH (Chem. Abstr.).

Effect of Pentobarbital and Ether on the Spreading Cortical Adpression. Van Harreveld, A., and Stamm, J. S. [*Am. J. Physiol.*, **173**, 164 (1953).]

A spreading depression of cortical activity is elicited in the rabbit by weak faradic stimulations of the cerebral cortex. The effects of ether and of pentobarbital on the slow potential change accompanying the spreading depression are parallel to the effects of these narcotics on depolarization potentials which can be led off from the spinal cord during asphyxiation.

E. D. WALTER (Chem. Abstr.).

Cerebral Asphyxiation and Spreading Cortical Depression. Van Harreveld, A., and Stamm, J. S. [*Am. J. Physiol.*, **173**, 171–5 (1953).]

Experimental support was found that the cortical asphyxiation potential of long latency and the slow potential change accompanying the spreading cortical depression are based on identical processes. E. D. WALTER (Chem. Abstr.).

Spectophotometric Diagnosis of Barbiturate Poisoning. Simonin, Métais, and Weil, [*Ann. méd. légale, criminol., police sci., méd. sociale, at toxicol.*, **32**, 372 (1952).]

Blood is treated with tungstic acid and the filtrate is extracted with $CHCl_3$. The difference in optical d. at 239 mμ of an aliquot adjusted to pH 10 and to pH 2 is proportional to the amount of barbiturate in the extraction.

ERICH HIRSCHBERG (Chem. Abstr.).

Equilibrium of Body Fluids in the Treatment of Chronic Alcoholism with Apomorphine. Feldmann, H. [*Rev. med. Suisse romande*, **72**, 205 (1952).]

Changes in biochemical compound of body fluids during apomorphine treatment are reviewed. New data on 50 cases are presented. Abnormal values became normal after apomorphine treatment. W. C. TOBIE (Chem. Abstr.).

Action of Strychnine on Spinal Mechanisms. Bernhard, Carl Gustaf. [*Anales inst. farmacol. españ.* (*Madrid*), **1**, 9–20 (1952).]

The effect of strychnine (I) on multisynaptic (II) and monosynaptic (III) reflexes varies with the degree of integrity of the central nervous system. Thus, low spinal preparations show augmentations of (II) and (III) by (I) at 0·14 mgm./kgm. High spinal preparations treated with 0·0012 mgm./kgm. of (I) show reductions in (III) but not (II). Large doses of (I) result in abolition of (III) and enhancement of (II) in high spinal preparations (I) augments both (II) and (III) in high spinal preparations which have been curarized. These data and the observed cord potentials are interpreted to indicate that (I) facilitates (II) and also stimulates higher spinal structures which inhibit (III). LEO SAPIRSTEIN (Chem. Abstr.).

The Hypnotic Action of p-Hydroxycamphor. Ogawa, Kazue. [*Folia Pharmacol. Japon.*, **48**, No. 4, 252 (1952).]

Of several central-nerve-stimulating camphor derivatives examined, p-hydroxycamphor was found to have a temporal hypnotic action by both subcutaneous and oral administration. This is probably not derived from its paralytic action but from a stimulating action on the sleeping center. Simultaneous administration of p-hydroxycamphor and evipan or cyclopentenylethyl-1-methylbarbituric acid showed a synergism, the latter diminishing the central-nerve-stimulating action of the former so that a natural sleep is produced. It is suggested that natural sleep is controlled by an antagonism between the sleeping and awakening centers.

S. KITAOKA (Chem. Abstr.).

Pharmacology of Vinylethynylcarbinols, a New Class of Central Nervous System Depressants. P'an, S. Y., et al. [*J. Pharmacol. Exptl. Therap.*, **107**, 459 (1953).]

3-Methylpent-1-yn-3-ol (methylparafynol), 3-methylpent-4-ene-1-yn-3-ol (I) (an intermediate in the compound synthesis of vitamin A), and 3-ethylpent-4-ene-1-yn-3-ol (II) are effective orally and parenterally as hypnotics in experimental animals. They act more rapidly than phenobarbital. (I) and (II) possess anticonvulsant activity against pentylenetetrazole seizures in mice, with protective indexes of 2·2 and 1·1 respectively. Their toxicity is low. Repeated daily doses in rats and dogs caused no ill effects. L. E. GILSON (Chem. Abstr.).

Pharmacological Properties of Benzazoles. II. Sites of Action in the Central Nervous System. Funderburk, W. H., et al. [*J. Pharmacol. Exptl. Therap.*, **107**, 356 (1953).]

2-Aminobenzothiazole (I) and its 4-methyl-, 4-chloro-, 6-methyl-, 6-chloro-, and 7-chloro-derivatives were studied in cats for their sites of action in the cerebrospinal axis from the brain stem to the lumbrosacral level of the spinal cord. Like bensimidazole, all of the compounds have a depressant effect on spinal interneurons. (I) showed a potency equal to that of mephenesin ; substitution at position 6 doubled the potency, and substitution at position 4 or 7 tripled it.

L. E. GILSON (Chem. Abstr.).

Influence of Substances Acting on the Autonomic System on the Threshold for Electroshock and Metrazole Convulsions. Wienke, H. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.* **217**,, 312 (1953).]

The threshold for electroshock by application of current for 0·1 and 1 seconds in rats and guinea-pigs and that to cardiazole are markedly lowered by adrenaline. Gynergen, doryl and nicotine had no significant influence on electroshock but lowered the threshold to cardiazole. Any lowering of the electroshock threshold was more evident in the tests with longer action of the current. Physostigmine, atropine, and pendiomid had no influence on either form of convulsions.

A. E. MEYER (Chem. Abstr.).